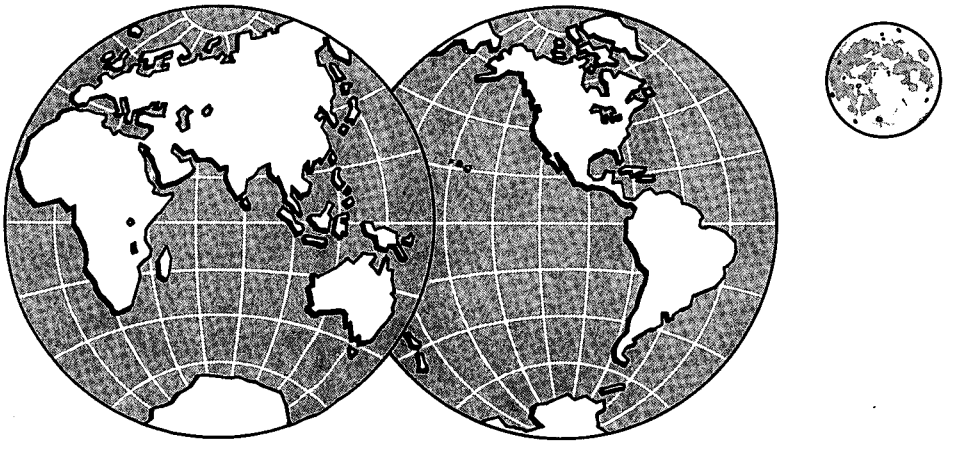
EPL 72-1

ENVIRONMENTAL PHYSIOLOGY LABORATORY

THE AUTOMATED PRIMATE RESEARCH LABORATORY (APRL)



UNIVERSITY OF CALIFORNIA - BERKELEY

ENVIRONMENTAL PHYSIOLOGY LABORATORY

UNIVERSITY OF CALIFORNIA, BERKELEY

THE AUTOMATED PRIMATE RESEARCH LABORATORY (APRL)

FINAL REPORT FOR

CONTRACT NSR 05-003-233 BETWEEN

THE NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

AND

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

Prepared by Nello Pace and G. Dale Smith

1 July 1972

APRL FINAL REPORT

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SECTION I.

INTRODUCTION

This report presents advance concepts and approaches for the implementation of a self-contained Automated Primate Research Laboratory (APRL). It presents concepts for science management and industry management participation. It presents a plan to develop both APRL and the University/industry management skills concurrently, by a logical division of projected effort to facilitate program funding and control.

The ultimate objective of this program was an extended space mission to define the physiological effects of weightlessness in a sub-human primate. Pioneering Phase I work for the Contract was accomplished in this laboratory under NASA Grant NGL 05-003-024, and was to be followed by a Phase II study under Contract NSR 05-003-233 to validate the preliminary APRL concept. Use of the APRL concept for a space mission was to have occurred in Phase III under the auspices of a NASA Development Center.

Termination of Contract funding on 30 June 1971 kept the University of California from completing Phase II. However, the following report is a summary of research, development, and management accomplished to date.

In the period of reduced funding for the past year, work has been continued under NASA Grant NGL 05-003-024 to develop breadboard hardware for a "monkey pod" to demonstrate its feasibility for a man-tended primate space flight experiment. Further information on this will be

found in the periodic reports of research activities supported by the Grant.

Contract NSR 05-003-233 "Automated Primate Research Laboratory" (APRL) was awarded to the Environmental Physiology Laboratory, University of California, Berkeley, on 27 June 1968 for research development studies to implement a primate space flight experiment, previously approved scientifically by the OSSA Space Biology Directorate of NASA. The product was to be a completely self-contained experiment module housing a pig-tailed monkey *(Macaca nemestrina)*, all necessary bioinstrumentation, and all life support for the animal. A further object was to translate experiment requirements into suitable engineering concepts leading to experiment requirement specifications and breadboard (prototype) models to demonstrate adequately flight experiment and hardware capabilities.

The work to be carried out fell into three categories:

A. Biological research needed to define proper monkey compatibility and interface.

B. Hardware concept development, production of prototypes, and tests to prove design.

C. Development of adequate management and contract monitoring capabilities to carry out subcontracting efforts with aerospace contractors.

However, in order to insure that hardware development completely subserved the maintenance of physiological integrity of the monkey and conduct of the physiological research, the APRL team was selected and organized so as to maximize transfer of all necessary design information between biologist and engineer. The APRL roster follows:

Nello Pace, Ph.D., Professor of Physiology, Principal Investigator

G. Dale Smith, D.V.M., APRL Project Manager

Robert N. Christenson, B.S.M.E., Engineering Development

Rutherford S. Gilfillan, M.D., Experimental Surgery

Benjamin W. Grunbaum, Ph.D., Biochemistry

Jens E. Hansen, B.S.E.E., Electrical Engineering

Neil M. Huber, D. rer. nat., Anthropology and Biostatistics

Arthur M. Kodama, Ph.D., Physiology

Norman C. Parrish, M.S.M.E., Bioinstrumentation and Design

Donald F. Rahlmann, Ph.D., Physiology

John R. Shively, B.M.E., Mechanical Engineering

Gene A. Spiller, D. Chem., Nutrition

N. Burwell G. Taylor, M.D., Ph.D., Science Coordination

Gerald A. Tolliver, M.A., Behavioral Psychology

Jack H. Wilmore, Ph.D., Physiology

This group of biomedical scientists and engineers was organized into a series of Working Groups for each subsystem of the APRL development. The Working Groups were made up of 4-6 members, at least one of whom was an engineer. In addition, Dr. N. B. G. Taylor served as Secretary for all Working Groups and attended all meetings to maximize coordination and cross-transfer of information. The 4 project engineers also met regularly as a separate group. The 8 Working Groups were as follows:

1. Monkey Subsystem
2. Nutrient Subsystem
3. Energy Metabolism Subsystem
4. Hemodynamics Subsystem
5. Restraint Subsystem
6. Feces Subsystem
7. Urine Subsystem
8. Data Handling Subsystem

Each of these areas involved special hardware problems, yet all had to be closely coordinated to the single animal subject of the experiment.

The following sections of the report describe the findings of each Working Group. At the end of the report is a Project Development Plan for APRL, and a Procurement Plan which would have been followed had the Contract continued. These last were the means for starting subcontract operations with the aerospace industry for fabrication of the various elements of the APRL system.

SECTION II.

REPORT OF THE APRL MONKEY SUBSYSTEM WORKING GROUP

Arthur M. Kodama, Chairman

N. Burwell G. Taylor, Secretary

Robert N. Christenson

Neil M. Huber

Donald F. Rahlmann

Gerald A. Tolliver

Jack H. Wilmore

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INTRODUCTION

The function of the monkey subsystem working group has been to compile under one cover, in as much detail as possible, the characteristics of the pig-tailed monkey *(Macaca nemestrina)*. This survey of behavioral, physical, and physiological parameters is to be a first cut at establishing a set of specifications to describe the monkey subsystem of the APRL study. The report is to be viewed as a preliminary document, to be updated with additional and better information as it becomes available.

As has been frequently stated, data on the pig-tailed monkey, particularly that which would have obvious bearing on APRL biology-engineering interfaces, is sparse. This report of the monkey subsystem working group consists primarily of a compilation of normal values and experimental data generated at the Environmental Physiology Laboratory, University of California, Berkeley, together with limited information from the literature.

Although the present report is concerned with the pig-tailed monkey, in certain critical APRL areas, e.g., gas metabolism and thermal environment, where little or no data is available, brief accounts of information on the closely related rhesus monkeys have been incorporated. Where experimental data is presented, no interpretation has been attempted. This survey has been limited to the male of the species.

The EPL PHAMOS Reports were the main sources of the data presented in this report. Much of the information in the PHAMOS Reports is nearly in raw data form, usually appearing later as summaries. Some of the

tables contained herein are taken directly from the PHAMOS reports. Others have been rearranged, retabulated, or summarized in the interest of a common format. As may be apparent from the table of contents, it was not always clear whether a particular piece of PHAMOS data should be included in this report because it represented solid information describing the pig-tailed monkey, or reported simply to indicate the variety of work that has been done on the animal.

A striking feature of the data gathered here is the limited use of statistical treatment. Measures of variance are reported whenever available, but for most part, description of the data is in terms of the number of observations, mean values, and ranges. It is presumed that most of the data will eventually be subjected to rigorous analysis, at which time the present collection of tables should be revised, at least to the extent of adding measures of standard deviation, standard error, etc.

Considerable help was obtained by the working group from the Primate Information Center at the University of Washington, Seattle, which provided a bibliography of physiological studies on the pig-tailed monkey. Some of the references were included in this report. However, many citations were excluded for reasons of (a) being too esoteric, e.g., "Neutrophil alkaline phosphatases in the blood cells of primates"; (b) having data difficult to comprehend or tabulate, e.g., "Synchronized spindle activity elicited in the cortex of the monkey by basal ganglion stimulation"; or (c) describing techniques, e.g., "Techniques for determination of cardiovascular response to exercise in unanesthetized monkeys." For the interested reader, a supplementary bibliography of these references has been included.

THE BEHAVIOR OF PIG-TAILED MONKEYS IN THEIR NATURAL HABITAT[1]

Pig-tailed monkeys *(Macaca nemestrina)* are found in Southeast Asia from the Naga Hills of Assam and Upper Burma, south through Thailand and Malaysia to Sumatra, Borneo, and the Andaman, Mentawai and Bangka Islands. They are among the most arboreal of the macaques (Napier & Napier 1967) and their habitat within this range is the deep rain forest. To what extent their occupation of this habitat reflects a response to predation by humans is not known, although the population is clearly disturbed and diminishing, and the species recently occupied wider territories. The monkeys are trapped for sale, and they are killed for food, because the natives fear them and because they depredate plantations and cultivated crops (Bernstein 1967). Apparently for these reasons, troops of pig-tails are shy of humans and difficult to observe. Thus, despite its importance for laboratory purposes, only one investigator, Bernstein, has published field studies of any detail concerning this species (Primate Information Center 1969), and an exhaustive search of the literature has failed to yield much ecological, ontological or behavioral information beyond that reported by him. Bernstein, himself, closely observed the behavior of only two troops, and cautioned that much of what he observed may have been influenced by the tension that his presence caused among the monkeys. The monkeys have long been exploited as coconut-pickers, however, and much information about them is available in this context (Gudger 1923), some of which is perhaps germane.

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1 See References 21-30.

ONTOGENY. Physically, the species appears to be variable; there are four subspecies (Napier & Napier 1967), while even within one village the captive animals were remarkably diverse (Corner 1956: "Some were short and thick...; others were long-haired...; while certain pale ones were considered the more aristocratic."). Presumably there is, therefore, rather great physiological and ontological individuality within the species. Nothing is reported concerning growth and development of these monkeys in the wild however. The closely-related *M. fascicularis* (the crab-eating macaque), which on the average is smaller and thus probably matures more rapidly than *M. nemestrina*, completes its permanent dentition at between seven and eight years of age and, although sexual maturity manifests itself at around four years, full growth is not completed until the tenth year in the males and the sixth year in females. The longevity record for *M. nemestrina* (albeit in a zoo) is 26 years and four months (Napier & Napier 1967).

ACTIVITY. According to Bernstein, he encountered his troops 40% of the time at medium levels in the trees and only 15% of the time on the ground; they were in multiple levels of the forest in 25% of his contacts and 15% of the time in the tops of the trees. They appeared most likely to come to the ground at midday and to remain in the highest trees during late evening hours or after dark and during the early morning. Travel was typically through low and medium trees in the early mornings and late afternoons. During rainy weather, activities continued much as usual except that during intense rain storms the animals often sat hunched over. Concerning captive monkeys employed as harvesters, Corner (1956) reported that they preferred trees from twenty to sixty feet tall, because of the greater abundance of insects they could obtain.

FEEDING. Bernstein called them the most omnivorous primates of the jungle, stating that the greater part of their daily activity is presumably spent in feeding and that they would feed sporadically through most of their waking hours. Again referring to captive animals, Corner (1956) reported: "Ceaselessly did the monkeys search for food; endless was their curiosity. Buds, opening shoots, limp young leaves, sticky hairs, dripping gums, flowers, fruits, watery interiors or unripe seeds, seedlings, fungus, caterpillers, cuckoo-spit, butterflies, moths, stick-insects, mantids, grasshoppers, spiders, spiders' webs, fresh termite mud, bees' nests, wasps' nests, birds' nests, eggs of all sorts from lizards' to snails', young birds, frogs, lizards -- in fact all the little fleshy and watery incidents in the forest were their food." This while on the end of a tether employed for the collection of botanical specimens.

SLEEPING. While there are no known reports of their sleeping behavior in their natural habitats, the monkeys presumably sleep in a peculiar sitting position in the smaller branches of high trees (Huber 1969).

SOCIAL PATTERNS. Their social patterns are reported in detail only by Bernstein, who, as mentioned, felt that what he observed may have been influenced by his presence. Apparently no behavior occurred that has not already been reported for pig-tailed monkeys observed in the laboratory (Kaufman and Rosenblum).

While solitary males are occasionally encountered, the monkeys usually live in troops consisting of animals of both sexes and all ages. One of the troops, the members of which Bernstein was actually able to count, consisted of around forty-five animals. As with other species of macaques, the organization of the troop is hierarchic, and orders of dominance

are continually established by punishment and threat of punishment (Bertrand 1967).

PREDATORS. The most important predator is man (Bernstein). "Snakes, panthers, and leopards keep the small monkeys chattering all night, and the shadow of the eagle haunts by day." (Corner).

TEMPERAMENT. Pig-tailed monkeys are usually savage animals and will inflict a nasty bite whenever they have the chance (La Rue 1919). "The males of the species are very savage and a friend of mine, who hunts all sorts and conditions of animals with a pack of mongrel dogs, told me that a brok (pig-tailed monkey) was the most dangerous of all to tackle; when at bay they stand with their backs to a tall tree and, seizing the dogs with hands or feet, slash and tear them with their terrible canine teeth, sometimes disembowelling them. The brok go around in droves, but often solitary males are to be found and these, I expect, have been driven from the leadership of their droves by younger and more powerful rivals . . . these solitary monkeys only . . . can be hunted by dogs for I do not suppose that any pack [of dogs] could deal with a drove . . ." (Shelford 1916). Bernstein (1967) says: "Dogs chased the two study troops on six occasions during the study.... A screaming juvenile hotly pursued by a dog brought the control male running and the control male tussled briefly with the dog before rejoining the group. The male seemed more than a match for the dog but the dogs were hunting in a small pack and continued their pursuit." Shelford calls the pig-tail "a highly intelligent animal", and as a pet "distinctly amusing" ... "but it must be kept in a cage or chained up, for ... it is ... the most wantonly destructive animal of my acquaintance." Corner (1956) mentions that they enjoy "breaking, smashing and knocking down" things.

TRAINING. Pig-tails can be trained to do almost anything, but to accomplish this the monkeys must be beaten severely whenever they fail to perform properly. Training is not based exclusively on punishment (Corner 1956) as has been reported (Bertrand 1967), however, for the monkey is rewarded by good feeding and companionship, and the Malay is emphatic that a good monkey must be one of the family (Corner 1956). Both Corner and Bertrand report that for training, preferably 1 or 2 year old male animals are trapped and, to establish his dominance, the man who obtains the monkey beats him. Beating may be necessary to reestablish dominance when a man has not worked with his monkey for several months. Apparently the monkey learns to respect and obey his trainer as he would a dominant male pig-tail in a pig-tail troop, in which dominance is similarly established by punishment and threat of punishment. The animals are in constant communication with their owners, sometimes through tugs on a tether, sometimes free, but appear in any case to respond to a variety of vocal commands and facial expressions. Corner suggests that they work partly through fear of punishment and partly through enjoyment of breaking or knocking things down. He feels that this quality can be exploited more widely than it is.

TABLE 1

Discrimination between Three-Dimensional Objects as Learned by a Pig-tailed Monkey *(M. nemestrina)*. (1)

DISC VS. STAR				SMALL DISC VS. LARGE DISC			
Block of 10 Trials	Disc Rewarded No. correct per 10 trials			Block of 10 Trials	Small Disc Rewarded No. correct per 10 trials		
	0-3	4-6	7-10		0-3	4-6	7-10
1-10			X*	1-10		X	
11-20			X	11-20		X	
				21-30		X	
				31-40		X	
	Stimulus Reversed: Star Rewarded			41-50		X	
				51-60		X	
				61-70			X
1-10		X		71-80			X
11-20			X				
					Stimulus Reversed: Large Disc Rewarded		
				1-10	X		
				11-20			X
				21-30		X	
				31-40		X	
				41-50		X	
				51-60		X	
				61-70		X	
				71-80	X		
				81-90			X
				91-100			X
				101-110			X
				111-120		X	

* X's indicate that the actual number of correct choices in the total of 10 trials fell into the range shown. The range (4-6) is taken to represent chance performance; i.e., the monkey could be choosing right or left consistently, or choosing the shapes randomly.

TABLE 2

Discrimination between Black and White Triangles as Learned by a Pig-tailed Monkey *(M. nemestrina)*. (1)

Block of 20 Trials	A Original Learning: White Triangle Rewarded No. correct per 20 trials			B First Reversal: Black Triangle Rewarded No. correct per 20 trials			C Second Reversal: White Triangle Rewarded No. correct per 20 trials		
	0-6	(7-13)	14-20	0-6	(7-13)	14-20	0-6	(7-13)	14-20
1-20		X*		X			X		
21-40		X		X			X		
41-60			X	X			X		
61-80			X	X			X		
81-100			X	X			X		
101-120			X	X				X	
121-140			X		X			X	
141-160		X			X			X	
161-180			X		X			X	
181-200		X			X			X	
201-220			X		X			X	
221-240			X		X			X	
241-260			X		X			X	
261-280			X		X			X	
281-300					X				X
301-320					X			X	
321-340					X			X	
341-360						X		X	
361-380					X				X
381-400					X				X
401-420						X			X
421-440						X			X
441-460					X				X
461-480						X			X
481-500						X		X	
501-520						X			X

* X's indicate that the actual number of correct choices in the total of 20 trials fell into the range shown. The range (7-13) is taken to represent chance performance; i.e., the monkey could be choosing right or left consistently, or choosing white or black randomly.

TABLE 3

Average Body Measurements (by weight) of Pig-tailed Monkeys *(M. nemestrina)*. (2)

Measurement	Unit	5-7 kg (n=17)	7-9 kg (n=25)	9+ kg (n=18)
Crown to base of tail	cm	42.2	45.8	48.0
Crown to tip of tail	cm	59.8	62.7	67.4
Sitting height (vertex to 1st caudal vertebra)	cm	37.2	40.3	43.6
Head circumference, occipital to supraoptic (above ears)	cm	30.2	33.0	35.1
Head length (prognathic)	cm	15.4	17.0	18.1
Head height (gonion to vertex)	cm	10.8	11.3	12.0
Head width (above ears)	cm	10.6	11.4	13.1
Inter-nostril breadth (septal)	cm	0.8	0.8	0.9
Interpupillary distance	cm	3.2	3.8	4.2
Neck circumference	cm	23.8	26.6	30.7
Neck width	cm	4.6	6.1	6.2
Shoulder circumference (deltoid muscles)	cm	41.6	44.1	52.4
Upper-arm circumference	cm	15.4	17.2	18.7
Midline around shoulder to tip of finger	cm	53.2	55.3	59.4
Humeral head to surface radial epicondyle	cm	16.8	17.6	18.9
Tip of olecranon to ulnar styloid	cm	18.9	19.8	20.9
Hand breadth, right	cm	5.2	5.5	5.7
Chest depth (manubrium to posterior spine)	cm	9.5	11.7	12.4
Chest depth (xiphoid to posterior spine)	cm	9.0	10.8	11.7
Circumference of chest at nipples	cm	33.6	37.6	41.8
Thorax (bi-deltoid)	cm	20.2	22.6	24.6
Thorax (bi-acromial)	cm	17.0	18.6	20.8
Circumference of abdomen at umbilicus	cm	28.4	32.7	38.6
Umbilical depth	cm	7.4	8.9	10.4
Hip circumference	cm	27.2	31.2	36.0
Bi-iliac crest	cm	11.9	12.6	13.9
Bi-ischial	cm	10.7	11.4	12.3
Maximum ischial callosity	cm	8.0	8.6	8.9
Distance between ischial callosity and line tangent to back	cm	2.2	2.5	2.3
Distance between anal aperture and 1st caudal vertebra	cm	3.3	3.6	4.0
Depth: iliac spine to vertebral column	cm	3.8	4.4	4.5
Depth at pubic symphysis	cm	6.0	7.1	7.5
Midline around hip to tip of toe	cm	56.4	60.1	64.2
Midthigh circumference	cm	19.6	22.5	23.9
Greater trochanter to knee joint	cm	18.6	19.3	20.7
Knee joint to lateral malleolus	cm	20.0	20.4	21.3
Calf circumference	cm	13.8	15.3	16.6
Foot breadth, right	cm	5.5	5.8	6.2
Shoulder width	cm	19.5	22.6	23.6
Right hand length	cm	15.7	16.3	15.9
Right foot length	cm	11.9	12.7	16.5
Body weight	kg	6.37	7.95	10.53
All 3rd molars erupted in	n	1/17	22/25	18/18

TABLE 4

Individual Organ Weights in 3 Pig-tailed Monkeys (M. nemestrina).(1)

	Number of Observations	Mean	Range
Adrenals (g/100 g BW)	2	0.019	0.018-0.020
Heart (g/100 g BW)	3	0.42	0.35-0.48
Lungs (g/100 g BW)	2	0.62	0.59-0.65
Liver & Gall Bladder (g/100 g BW)	3	2.17	1.47-2.93
Spleen (g/100 g BW)	2	0.14	0.12-0.16
Kidneys (g/100 g BW)	3	0.39	0.29-0.58
Seminal Vesicles (g/100 g/BW)	3	0.29	0.18-0.39

TABLE 5

Average Body Measurements of Growing Pig-tailed Monkeys (M. nemestrina) of Known Age. (2)

Age		12 mos.	24 mos.	36 mos.	48 mos.
No. of Animals		4	3	2	2
Measurements	(Units)				
Crown to base of tail	(cm)	33.9	40.2	39.0	--
Crown to tip of tail	(cm)	46.6	49.2	57.1	--
Midline around shoulder to tip of finger	(cm)	32.8	41.7	45.9	46.1
Midline around hip to tip of toes	(cm)	35.4	45.8	48.4	52.0
Greater trochanter to knee joint	(cm)	10.4	12.7	15.4	16.8
Knee joint to lateral malleolus	(cm)	10.8	13.3	15.3	17.6
Humeral head to surface radial eipcondyle	(cm)	9.5	12.0	13.9	15.5
Tip of olecranon to ulnar styloid	(cm)	10.7	13.3	13.8	16.7
Circumference of head occipital to supraoptic (above ears)	(cm)	23.9	26.4	26.5	27.0
Circumference of chest at nipples	(cm)	22.2	26.5	28.5	31.7
Circumference of abdomen at naval	(cm)	17.8	22.3	23.9	26.8
Interpupillary distance	(cm)	2.3	2.8	3.0	3.0
Width of head above ears	(cm)	6.5	6.9	6.9	9.3
Length of hand, right	(cm)	7.8	8.9	10.3	11.1
Length of hand, left	(cm)	7.8	8.9	10.3	11.0
Length of foot, right	(cm)	11.1	12.8	14.4	15.1
Length of foot, left	(cm)	11.1	12.8	14.5	15.1
Body Weight	(kg)	1.97	2.85	3.44	4.50

TABLE 6

Age in Months of the Appearance of Ossification Centers in 5 Pig-tailed Monkeys (M. nemestrina). (2)

Center of Ossification		Mean	Range
Humerus	Proximal Epiphyses	P*	
Humerus	Distal Epiphyses	P	
Humerus	Medial Epiphyses	1	0-2
Radius	Proximal Epiphyses	2	0-4
Ulna	Proximal Epiphyses	4	2-9
Radius	Distal Epiphyses	P	
Ulna	Distal Epiphyses	P	
Carpals		P	
Metacarpals	Epiphyses	P	
Phalanges	Proximal Row Epiphyses	P	
Sesamoids	Radial Carpal	42	42-43
Sesamoids	First Digital	33	28-42
Femur	Proximal Epiphyses	P	
Femur	Lesser Trochanter	9	8-11
Femur	Distal Epiphyses	P	
Patella		13	12-15
Fabellae		45	
Tibia	Proximal Epiphyses	P	
Tibia	Tuberosity	45	
Fibula	Distal Proximal Epiphyses	22	18-24
Tibia	Distal Epiphyses	P	
Fibula	Distal Epiphyses	P	
Tarsals		P	
Calcaneus	Epiphyses	22	18-28
Metatarsals	Epiphyses	P	
Phalanges	Proximal Row Epiphyses	P	
Sesamoids	Lateral Tarsal	43	
Sesamoids	Radial Tarsal		52
Sesamoids	First Digital Proximal	32	25-40
Sesamoids	First Digital Distal	42	42-52
Sesamoids	Fifth Digital		52
Sesamoids	2nd - 4th Digital	46	

* P = Probably present at birth

TABLE 7

Earliest Observed Age in Months of Completed Epiphyseal Closures in the Pig-tailed Monkey (M. nemestrina). (2)

Center of Ossification		
Humerus	Proximal Epiphyses	> 52
Humerus	Distal Epiphyses	40
Humerus	Medial Epiphyses	49
Radius	Proximal Epiphyses	> 52
Ulna	Proximal Epiphyses	> 52
Radius	Distal Epiphyses	> 52
Ulna	Distal Epiphyses	> 52
Metacarpals	Epiphyses	> 52
Phalanges	Proximal Row Epiphyses	> 52
Femur	Proximal Epiphyses	> 52
Femur	Lesser Trochanter	> 52
Femur	Distal Epiphyses	> 52
Tibia	Proximal Epiphyses	> 52
Tibia	Tuberosity	> 52
Fibula	Proximal Epiphyses	> 52
Tibia	Distal Epiphyses	> 52
Fibula	Distal Epiphyses	> 52
Calcaneus	Epiphyses	> 52
Metatarsals	Epiphyses	> 52
Phalanges	Proximal Row Epiphyses	> 52

TABLE 8

Hemodynamic Measurements of 16 Pig-tailed Monkeys (M. nemestrina). (3)

Measurement	No. of Measurements Included in Mean	Mean	Standard Deviation	Range Low	Range High
Body Weight (kg)		8.04	1.21	6.50	9.89
Respiratory Rate (breaths/min)	756	34	6	23	44
Heart Rate (beats/min)	756	193	16	168	223
Aortic Systolic Pressure (torr)	748	127	15	104	166
Aortic Diastolic Pressure (torr)	748	76	9	55	90
Aortic Pulse Pressure (torr)	748	51	11	37	68
Aortic Mean Pressure (torr)	756	100	11	83	115
Venous Mean Pressure (torr)	550	-0.6	1.4	-2.3	$\pm$ 2
Left Atrial Mean Pressure (torr)	208	-0.9	1.2	-2.9	0.7
Pulmonary Arterial Mean Pressure (torr)	74	16.5	3.5	13.0	23.5
Cardiac Output	378				
ml/min		968	248	623	1,437
ml/kg/min		122	23	90	171
Stroke Volume (ml)	378	5.4	1.3	3.1	12.0
Systemic Resistance (dyne sec/cm^5)	378	8,505	2,210	6,304	12,416
Left Ventricular Power (watts)	378	.216	.069	.118	.351
Pulmonary Resistance (dyne sec/cm^5)	74	1,313	578	835	2,404
Right Ventricular Power (watts)	74	.039	.011	.021	.054

TABLE 9

Heart Rate, Respiratory Rate, and Blood Pressure Data from Unanesthetized and Anesthetized Pig-tailed Monkeys (M. nemestrina). (1)

	Unanesthetized			Anesthetized		
	n	Mean	Range	n	Mean	Range
Heart Rate (beats/min)	12	201	138-258	4	136	114-190
Respiratory Rate (breaths/min)	12	32	18-48	2	28	26-30
Aorta Systolic Pressure (torr)	12	141	105-203	4	116	88-147
Aortic Diastolic Pressure (torr)	12	92	62-158	4	75	66-107
Aorta Pulse Pressure (torr)	12	50	24-67	4	41	22-49
Aorta Mean Pressure (torr)	12	112	83-137	4	--	81-128

TABLE 10

Hemodynamic Summary of a Pig-tailed Monkey (M. nemestrina) at 750 and 460 torr Ambient Pressures. (1)

	750 torr			460 torr		
	n	Mean	Range	n	Mean	Range
Respiratory Rate (breaths/min)	14	19	16-22	3	29	27-30
Heart Rate (beats/min)	23	177	157-198	24	167	156-180
Aortic Systolic Pressure (torr)	22	134	126-142	24	118	112-127
Aortic Diastolic Pressure (torr)	22	86	82-93	24	74	66-80
Aortic Pulse Pressure (torr)	22	48	46-52	24	44	41-52
Aortic Mean Pressure (torr)	22	111	100-117	24	98	85-105
Cardiac Output (ml/min)	15	832	738-979	11	944	868-1,144
Stroke Volume (ml)	12	4.8	4.0-6.1	11	5.6	5.2-6.4
Systemic Resistance ($\frac{dyne}{sec/cm^5}$)	12	10,663	9,397-11,910	11	8,301	6,643-9,460
Cardiac Work (watts)	12	0.211	0.185-0.250	11	0.204	0.165-0.241

TABLE 11

Cardiovascular Changes in a Pig-tailed Monkey (M. nemestrina) with slow infusion of epinephrine and norepinephrine. (1)

	Control			Epinephrine (10 μg/min for 2.5 min)			Norepinephrine (6 μg/min for 1.5 min)		
	n	Mean	Range	n	Mean	Range	n	Mean	Range
Heart Rate (beats/min)	8	143	133-155	3	157	150-160	3	94	84-102
Aortic Systolic Pressure (torr)	8	122	120-125	3	135	133-138	3	162	158-168
Aortic Diastolic Pressure (torr)	8	79	74-81	3	72	70-75	3	91	90-93
Aortic Pulse Pressure (torr)	8	44	41-48	3	63	61-65	3	71	68-75
Aortic Mean Pressure (torr)	8	101	100-103	3	101	100-102	3	121	118-125
Aortic Flow (liters/min)	8	1.72	1.60-1.84	3	2.23	2.10-2.35	3	1.46	1.42-1.48
Stroke Volume (ml)	8	12.1	10.9-13.1	3	14.2	14.0-14.7	3	15.6	14.4-16.9
Systemic Resistance (dyne sec/cm^5)	8	4740	4450-5060	3	3630	3470-3830	3	6660	6420-7050
Cardiac Work (watts)	8	0.385	0.370-0.416	3	0.499	0.468-0.532	3	0.391	0.382-0.395

TABLE 12

Hemodynamic Effects of Hypothermia on a Pig-tailed Monkey (M. nemestrina).(1)

Time of Day	Esophageal Temp. (C)	Rectal Temp. (C)	Respiratory Rate (breaths/ min)	Aortic Pressures				Heart Rate (beats/ min)	Cardiac Output (liters/ min)	Stroke Volume (ml)	Systemic Resistance (dyne sec/ cm^5)	Cardiac Work (watts)
				Systolic (mm Hg)	Diastolic (mm Hg)	Pulse (mm Hg)	Mean (mm Hg)					
1126	34.9	35.2	20	157	112	45	136	172	0.67	3.9	16,200	.202
1142	33.7	34.0	17	141	97	44	121	156	0.57	3.7	17,000	.153
1153	31.6	31.9	16	152	106	46	127	132	0.54	4.1	18,800	.139
1208	29.9	29.9	14	155	107	48	132	120	0.46	3.8	23,000	.135
1222	28.2	28.4	14	152	107	45	130	92	0.33	3.6	31,600	.095
1233	26.8	27.0	16	155	106	49	127	80	0.30	3.8	34,000	.085
1247	25.3	25.6	12	142	100	42	125	76	0.27	3.6	37,100	.075

TABLE 13

Cerebral Blood Flow and Metabolism in Pig-tailed Monkeys (M. nemestrina) During Various Procedures.(4)

Procedure	No. of Animals		Cerebral Blood Flow (ml/100g brain/min)		Cerebral Glucose Consumption (mg/100 g brain/min)	
			C	E	C	E
100% O_2 Inhalation	7	Mean	60.8	53.5	3.03	2.81
		S.D.	9.8	9.9	0.87	0.51
5% CO_2 + Air Inhalation	5	Mean	63.2	90.3	4.77	6.95
		S.D.	4.1	10.5	1.53	1.03
20% CO_2 + O_2 Inhalation	3	Mean	49.1	105.9	3.00	3.58
		S.D.	15.3	23.5	0.82	1.45
Hyperventilation	5	Mean	44.6	28.4	2.40	3.15
		S.D.	7.0	7.4	0.71	1.85
7% O_2 + N_2 Inhalation	6	Mean	52.5	59.1	3.40	6.32
		S.D.	12.7	9.1	0.94	2.84
100% N_2 Inhalation	3	Mean	50.9	79.5	3.76	7.93
		S.D.	8.8	17.8	0.30	1.79

Note: C = control period; E = experimental period.

TABLE 14

Dynamic Ranges for Heart Rate and Mean Aortic and Pulmonary Artery Blood Pressures Before and During Centrifugation (up to 12 G) in 6 Pig-tailed Monkeys (M. nemestrina). (1)

	Heart Rate (beats/min)	Blood Pressure, torr	
		Aortic	Pulmonary Artery
Before (rest)	165-230	82-130	9 - 16
Centrifugation (up to 12G)	195-250	130-259	9 - 102

TABLE 15

Metabolic Gas Exchange and Heat Production by a 10 kg Pig-tailed Monkey (M. nemestrina). (5)

	Day Active	Day Quiet	Night Dozing
O_2 Consumption (liters/hr)	12.6	4.9	4.4
CO_2 Production (liters/hr)	10.8	4.3	3.6
Respiratory Quotient (CO_2/O_2)	0.86	0.88	0.82
Heat Production (kcal/hr)	62.2	24.1	21.1
Heat Production (kcal/day/$BW^{3/4}$)	261.3	101.6	91.4

TABLE 16

Literature Values of Metabolic Rate for the Rhesus Monkey (M. mulatta).(6,7,8)

Reference	Condition	n	Body Weight (kg)	Metabolic Rate (kcal/day/$BW^{3/4}$)
Bruhn	Sleep	3	3.7-8.1	67.91
Benedict	Basal	14	3.3-5.1	68.60
Rakieten	Rest	11	2.7-3.7	64.77

TABLE 17

Ventilatory and Related Blood Chemistry Data on Two Pig-tailed Monkeys (M. nemestrina) Breathing Room Air During Continuous Restraint. (1)

	Number of Observations	Mean	Range
Minute Volume (liters/min.)	47	3.06	2.29-4.10
Tidal Volume (liters)	47	0.083	0.060-0.106
Respiratory Rate (breaths/min.)	79	37	24-25
Arterial P_{O_2} (torr)	71	88	81-97
Arterial pH	38	7.46	7.45-7.58

TABLE 18

Blood Gas Analysis in 6 Pig-tailed Monkeys (M. nemestrina). (1)

	Number of Observations	Mean	Range
Aorta			
P_{O_2} (torr)	12	107.6	102.5-115.0
P_{CO_2} (torr)	12	37.1	35.0-41.5
pH	12	7.486	7.475-7.503
Pulmonary Artery			
P_{O_2} (torr)	12	36.6	32.0-43.5
P_{CO_2} (torr)	12	44.6	38.8-49.3
pH	12	7.431	7.415-7.455

TABLE 19

Changes in Aortic Partial Pressure of Oxygen with Varying Ambient Air Pressures Recorded from a Chronically Implanted Sensor in a Pig-tailed Monkey (M. Nemestrina).(1)

Ambient Air Pressure (torr)	Oxygen Partial Pressures			Saturated Air pO_2 minus Aortic Blood pO_2 (torr)
	Dry Air (torr)	Saturated Air (torr)	Aortic Blood (torr)	
754	157	147	92	55
700	146	135	82	53
650	135	12	76	49
600	125	115	67	48
550	114	104	52	52
500	104	94	44	50
450	94	84	38	46
425	87	78	35	43
450	94	84	37	47
500	104	94	39	55
550	114	104	50	54
600	125	115	58	57
650	135	125	70	55
700	146	135	85	50
754	157	147	102	45

TABLE 20

Oxygen-Hemoglobin Dissociation Curve Data for 6 Pig-tailed Monkeys (M. nemestrina). (1)

pO_2 (torr)	Per cent saturation of hemoglobin at various levels of oxygen partial pressure.		
	Mean	S.D.	Range
14	19.8	2.8	17.9-23.6
24	32.8	2.3	29.0-37.5
31	45.2	1.8	40.4-47.5
42	63.2	3.8	55.5-68.0
56	83.7	2.2	77.7-86.2
71	92.2	3.8	86.8-97.2
85	97.8	1.1	93.7-100.0

TABLE 21

Respiratory Properties of Blood in the Pig-tailed Monkey (M. nemestrina).(9)

	No. of Animals	Mean	S. D.	Range
O_2 Transport				
O_2 Capacity (Vol %)	8	16.6	2.0	12.7-18.4
P_{50} (torr)	8	36.7	1.1	35.5-38.2
Bohr Effect	8	-0.520	0.032	-0.474--9.544
CO_2 Transport				
Bicarbonate (mM/liter)	8	24.7	2.1	21.5-27.8
CO_2 Combining power (vol %)	8	44.0	2.1	41.2-46.5
Haldane Effect (vol %)	8	4.5	0.6	3.2 - 5.1

O_2 capacity = oxygen bound to hemoglobin when P_{O_2} is 150 torr.

P_{50} = partial pressure of oxygen corresponding to 50% saturation when pH is 7.4.

Bohr effect = $\Delta \log P_{O_2} / \Delta pH$.

Standard bicarbonate = bicarbonate concentration in plasma when P_{CO_2} is 40 torr. and the hemoglobin is totally saturated.

CO_2 combining power = total CO_2 content in whole oxygenated blood when P_{CO_2} is 40 tor

Haldane effect = CO_2 added when oxygenated whole blood is totally reduced at a PCO_2 of 40 torr.

TABLE 22

Hematological Values from 26 Pig-tailed Monkeys (M. nemestrina). (10)

	Mean	Standard deviation	Range
Body Weight (kg)	8.6	1.6	5.9-11.7
Leukocyte count ($10^3/mm^3$)	11.78	2.65	8.50-16.71
Lymphocytes (%)	44.9	3.9	37.0-51.2
Monocytes (%)	2.3	1.7	0.5-8.0
Neutrophils (%)	50.1	3.4	44.8-58.3
Eosinophils (%)	2.0	1.5	0.0-5.1
Basophils (%)	0.7	0.6	0.0-3.0
Erythrocyte count ($10^6/mm^3$)	5.95	0.57	4.75-7.01
Hematocrit value (%)	41.8	4.82	31.0-47.5
Hemoglobin (g/100 ml blood)	11.3	1.3	8.5-14.2
Mean corpuscular volume (μm^3)	70.4	6.2	60.8-85.4
Mean corpuscular hemoglobin ($\mu\mu g$)	19.0	1.7	16.3-24.4
Mean corpuscular hemoglobin concentration (%)	27.1	2.3	22.1-30.5
Erythrocyte diameter (μm)	7.2	0.3	6.6-7.6

TABLE 23

Hematological Changes in 8 Pig-tailed Monkeys (M. nemestrina) During 30-180 Days of Exposure to an Altitude of 3,800 Meters (474 torr Ambient Air Pressure). (1)

	Sea Level			3,800 Meters		
	Number of Observations	Mean	Range	Number of Observations	Mean	Range
Hemoglobin (g/100ml)	32	13.6	10.0-16.5	8	19.3	17.4-22.3
Venous Hematocrit (%)	32	44.4	38.2-49.1	8	64.5	56.6-79.1
Red Blood Cell Count ($\times 10^6/mm^3$)	32	5.99	4.45-8.05	8	8.83	7.32-10.40
White Blood Cell Count ($\times 10^3/mm^3$)	32	15.75	5.90-30.60	8	10.13	4.45-17.80

TABLE 24

Mean Hematological Data from 4 Pig-tailed Monkeys (M. nemestrina) During 90 Days on Mixed Natural Foodstuffs (Compared with Mean Values on Commercial Monkey Chow and on Canned Complete Liquid Diet). (11)

	Natural foodstuffs	Purina monkey chow	Vanilla Nutrament
Hematocrit value (%)	46.5	41.8	45.3
RBCx10^6/mm^3	6.82	5.95	6.44
WBCx10^3/mm^3	12.7	11.78	11.5
Hemoglobin (gm%)	13.7	11.3	12.4
Mean Corpuscular Hemoglobin (µµg)	20.1	19.0	19.3
Mean Corpuscular Hemoglobin Concentration (%)	29.5	27.0	27.4
Plasma glucose (mg%)	84.5	73.0	--
Total plasma protein (gm%)	7.7	7.3	7.2
Plasma albumin (gm%)	3.5	3.5	3.8

TABLE 25

Blood Constituents in Pig-tailed Monkeys (M. nemestrina).(1,12)

	No. of Animals	Mean	Range
Serum Sodium (meq/liter)	93	149	136-162
Serum Potassium (meq/liter)	93	4.2	3.0-6.2
Serum Chloride (meq/liter)	93	110	100-118
Serum Bicarbonate (meq/liter)	73	22.7	15.0-29.3
Serum Phosphorus (mg/100 ml)	10	6.3	5.4-6.9
Plasma Glucose (mg/100 ml)	47	86	50-138
Blood Urea Nitrogen (mg/100 ml)	47	20	8-37

TABLE 26

Plasma Proteins in Intact Pig-tailed Monkeys (M. nemestrina).(1)

	Number of Observations	Mean	Range
Total Protein (g/100 ml)	8	7.23	5.81-8.45
Albumin (g/100 ml)	8	3.84	3.16-4.33
Total Globulins (g/100 ml)	8	3.31	2.31-4.37
α_1 Globulin (g/100 ml)	8	0.40	0.12-0.64
α_2 Globulin (g/100 ml)	6	0.43	0.15-0.70
β_1 Globulin (g/100 ml)	8	0.56	0.35-0.94
β_2 Globulin (g/100 ml)	7	0.55	0.33-0.79
γ Globulin (g/100 ml)	8	0.82	0.41-1.04
Fibrinogen (g/100 ml)	8	0.75	0.46-1.03
A/G Ratio	8	1.18	0.88-1.70

TABLE 27

Plasma Proteins in Chronically Catheterized Pig-tailed Monkeys (M. nemestrina). (1)

	Number of Animals	Mean	Range
Total Protein (g/100 ml)	10	7.36	6.50-8.20
Albumin (g/100) ml)	10	2.29	1.92-2.48
Total Globulins (g/100 ml)	10	3.78	3.24-4.08
α_1 Globulin (g/100 ml)	10	0.80	0.66-1.03
α_2 Globulin (g/100 ml)	10	0.62	0.20-1.01
β_1 Globulin (g/100 ml)	7	0.69	0.56-0.79
β_2 Globulin (g/100 ml)	7	0.47	0.22-0.99
γ Globulin (g/100 ml)	10	1.29	0.80-1.76
Fibrinogen (g/100 ml)	10	1.28	0.94-1.79
A/G Ratio	10	0.58	0.29-0.75

TABLE 28

Water Intake and Urine Output in Pig-tailed Monkeys (M. nemestrina).(1)

	No. of Animals	Mean	Range
Body Weights (kg)	19	7.19	4.31-10.65
Water Intake (ml/day)	19	631	394-760
Urine Output (ml/day)	19	295	169-518

TABLE 29

Six-Hour Urine Volume Measurements (ml) in 5 Bilateral Ureteral Catheterized Pig-tailed Monkeys (M. nemestrina). (1)

	Number of Observations	Mean	Range
Right Ureter 0000-0600	69	47	5-190
0600-1200	34	73	1-119
1200-1800	77	47	3-207
1800-2400	74	44	1-213
Left Ureter 0000-0600	74	52	5-188
0600-1200	77	40	9-121
1200-1800	80	54	4-170
1800-2400	78	45	10-182
Total, Both Catheters, 24 Hours	59	327	121-666

TABLE 30

Continuous (Hourly) pH Measurements with a Flow-Through Electrode on a Bilateral Ureteral Catheterized Pig-tailed Monkey (M. nemestrina) While in an Upright or Supine Position.(1)

Day Post-Surgery	Mean pH Upright	Mean pH Supine	Difference (Upright-Supine)
4	5.20	5.12	0.08
5	5.36	6.00	-0.64
6	5.94	6.99	-1.05
7	6.30	6.34	-0.04
8	6.45	5.80	-0.65
9	5.97	6.67	-0.70
10	6.25	6.74	-0.49
11	6.72	6.90	-0.18
12	6.75	7.09	-0.34
13	6.86	7.01	-0.15
14	6.75	7.06	-0.31
15	6.72	6.95	-0.23
16	6.00	6.24	-0.24
17	6.56	6.73	-0.17
18	6.14	6.67	-0.53
19	6.06	6.46	-0.40
20	5.74	5.82	-0.08
21	6.19	6.50	-0.31
22			
23	6.73	7.10	-0.37
24	6.95	7.20	-0.25
25	6.55	6.70	-0.15
26	6.35	6.75	-0.40

con't

27	6.10	6.56	-0.46
28	6.45	6.32	-0.13
29	6.45	6.65	-0.20
30	6.05	5.92	0.13
31	6.41	6.50	-0.09
32	6.00	6.17	-0.07
33	6.40	5.82	0.58
34	5.85	6.07	-0.22
35	5.67	5.75	-0.08
36	5.74	5.81	-0.07
37	5.87	6.27	-0.40
38	6.27	6.16	-0.11
39	5.87	6.10	-0.20
40	5.87	6.11	-0.24
41	5.85	5.94	-0.09

Note: The animal was fed Purina Chow and water ad libitum.

TABLE 31

Hourly Excretion Rates of Various Urinary Constituents in 3 Pig-tailed Monkeys (M. nemestrina). The Urine Was collected by Means of Bilateral Ureteral Catheterization. (1)

	No. of Observations	Mean	Range
Urine Output Rate (ml/hr)	116	19.8	5.0-40.7
Specific Gravity	116	1.012	1.005-1.022
Total Osmotic Activity (milliosmols/hr)	116	5.92	1.55-13.90
pH	116	7.06	5.60-8.17
Sodium (mmoles/hr)	116	0.31	0.01-1.47
Potassium (mmoles/hr)	116	0.60	0.22-1.16
Na/K	116	0.58	0.10-2.08
Calcium (mmoles/hr)	116	0.04	0.01-0.12
Magnesium (mmoles/hr)	116	0.05	0.00-0.12
Chloride (mmoles/hr)	116	0.45	0.02-1.40
Phosphate (mmoles/hr)	116	0.08	0.00-0.28
Sulfate (mmoles/hr)	116	0.22	0.06-0.48
Ammonia (mmoles/hr)	116	0.24	0.01-0.78
Urea (mmoles/hr)	116	4.52	1.32-8.34
Urate (μmoles/hr)	114	1.65	0.01-11.92

(con't)

TABLE 31 (continued)

Creatine (mmoles/hr)	116	0.04	0.00-0.12
Creatinine (mmoles/hr)	116	0.10	0.03-0.21
Creatine/Creatinine	92	0.36	0.03-1.95
OH-Proline (μmoles/hr)	48	6.7	1.0-13.5
Citrate (μmoles/hr)	47	7.2	0.9-23.7
Glucose (mmmoles/hr)	116	0.04	0.00-0.20
17 Ketosteroids (μmoles/hr)	116	1.24	0.14-2.84
17-OH Steroids (μmoles/hr)	116	0.67	0.01-2.90
5-OH Indoleacetate (μmoles/hr)	72	0.73	0.01-1.67
Epinephrine (nmoles/hr)	24	3.99	0.60-7.26
Norepinephrine (nmoles/hr)	24	13.18	2.66-21.81

Note: The animals were fed Purina Chow and water ad libitum.

TABLE 32

Analyses of Urine from 5 Pig-tailed Monkeys (M. nemestrina) Collected by Surgically Implanted Bladder Catheters. (1)

	Number of Observations	Mean	Range
Urine Output Rate (ml/hr)	67	13.52	3.3 - 43.3
pH	70	6.7	4.7 - 8.6
Specific Gravity	67	1.019	1.009 - 1.026
Calcium (mmoles/liter)	70	4.75	0.20 - 16.48
Urea (mmoles/liter)	70	397	44 - 607
Creatine (mmoles/liter)	65	5.21	0.01 - 34.48
Creatinine (mmoles/liter)	70	7.91	2.12 - 24.11

TABLE 33

Analyses of Urine from 4 Pig-tailed Monkeys (M. nemestrina) Collected in a Metabolic Cage.(1)

	Number of Observations	Mean	Range
Urine Output Rate (ml/hr)	51	10.1	0.9 - 24.4
pH	51	7.6	6.4 - 8.7
Specific Gravity	51	1.017	1.010 - 1.025
Calcium (mmoles/liter)	51	4.20	0.49 - 13.51
Urea (mmoles/liter)	51	268	114 - 465
Creatine (mmoles/liter)	51	1.82	0.11 - 5.84
Creatinine (mmoles/liter)	51	9.68	1.19 -17.46

Note: The animals were fed Purina Chow and water ad libitum.

TABLE 34

Mean Weekly Urinary Excretion of Calcium and Phosphorus in Pig-tailed Monkeys (M. nemestrina) on Two Types of Diets During Restraint and Non-restraint for a Period of 5 Weeks. (13)

	Number of Animals	Mean	Range
Urinary Calcium (mg/day)			
Unrestrained, A Diet	4	80	58-112
Restrained, A Diet	4	40	12-71
Unrestrained, B Diet	4	130	75-158
Restrained, B Diet	4	83	18-136
Urinary Phosphorus (mg/day)			
Unrestrained, A Diet	4	56	47-71
Restrained, A Diet	4	65	38-103
Unrestrained, B Diet	4	6	2-20
Restrained, B Diet	4	84	11-146

Note: The two diets were similar in provision of calories but differed in content of major nutrients. Diet A surpassed Diet B in protein, but was exceeded by Diet B in fat, CHO, and major minerals. Calcium was approximately three times as high in Diet B.

TABLE 35

Mean Weekly Fecal Excretion of Calcium and Phosphorus in Pig-tailed Monkeys (M. nemestrina) on Two Types of Diets During Restraint and Non-restraint for a Period of 5 Weeks. (13)

	Number of Animals	Mean	Range
Fecal Calcium (mg/day)			
Unrestrained, A Diet	4	163	153-184
Restrained, A Diet	4	205	173-231
Unrestrained, B Diet	4	790	597-894
Restrained, B Diet	4	986	301-1574
Fecal Phosphorus (mg/day)			
Unrestrained, A Diet	4	277	246-298
Restrained, A Diet	4	311	155-420
Unrestrained, B Diet	4	542	393-595
Restrained, B Diet	4	587	169-917

Note: The two diets were similar in provision of calories but differed in content of major nutrients. Diet A surpassed Diet B in protein, but was exceeded by Diet B in fat, CHO, and major minerals. Calcium was approximately three times as high in Diet B.

TABLE 36

Mean Weekly Body Weights and Urinary Excretion of Nitrogen in Pig-tailed Monkeys (M.nemestrina) on Two Types of Diets During Restraint and Non-restraint for a Period of 5 Weeks. (14)

	Number of Animals	Mean	Range
Body Weight (Per cent of initial weights)			
Unrestrained, A Diet	4	102	98-108
Restrained, A Diet	4	86	77-95
Unrestrained, B Diet	4	103	98-107
Restrained, B Diet	4	89	85-93
Nitrogen Excretion (Per cent of initial values)			
Unrestrained, A Diet	4	142	128-156
Restrained, A Diet	4	144	106-166
Unrestrained,B Diet	4	110	98-117
Restrained, B Diet	4	127	102-157

Note: The two diets were similar in provision of calories but differed in content of major nutrients. Diet A surpassed Diet B in protein, but was exceeded by Diet B in fat, CHO, and major minerals. Calcium was approximately three times as high in Diet B.

TABLE 37

Mean Weekly Urinary Excretion of Creatine and Creatinine in Pig-tailed Monkeys (M. nemestrina) on Two Types of Diets During Restraint and Non-restraint for a Period of 5 Weeks. (14)

	Number of Animals	Mean	Range
Creatine Excretion (mg/day)			
Unrestrained, Diet A	4	19	5-35
Restrained, Diet A	4	57	23-82
Unrestrained, Diet B	4	11	4-26
Restrained, Diet B	4	55	2-98
Creatinine Excretion(mg/day)			
Unrestrained, Diet A	4	284	265-305
Restrained, Diet A	4	209	165-260
Unrestrained, Diet B	4	275	260-280
Restrained, Diet B	4	290	245-365

Note: The two diets were similar in provision of calories but differed in content of major nutrients. Diet A surpassed Diet B in protein, but was exceeded by Diet B in fat, CHO, and major minerals. Calcium was approximately three times as high in Diet B.

TABLE 38

Hormonal Changes in the Pig-tailed Monkey (M. nemestrina) During Simulated Space Stresses. (15)

	Number of Animals	Urine Volume (ml/day)	Catechol Amine (ug/100ml)	17-Ketogenic Steroid (ug/day)
Mean Control	3	440	12	10.0
Mean Centrifuge		128	17	4.2
Mean Control	3	602	4	12.5
Mean Isolation		205	10	4.4
Mean Control	3	586	8	9.2
Mean Vibration		226	15	3.2

Centrifuge: A typical simulated launch profile was used for these studies with the centrifugal force applied ventrodorsally. The animal was accelerated to 7 G in 5 minutes, sustained at 7 G for 2 minutes, and decelerated to stop within 30 seconds. Above values for day following centrifugation.

Isolation: The animals were isolated in a sound-attenuated, light-proof box for a period of 14 days. The above measurements were made on the 15th day.

Vibration: Each animal was vibrated in three planes at right angles over a spectrum from 5 to 40 cycles/second, in continuous sweeps of ascending and descending frequency. The acceleration was maintained at 0.25 inch double amplitude from 5 to 13 cycles/second, and then changed to a constant acceleration of 2 G peak to peak to a maximum frequency of 40 cycles/second. Above values for day following vibration.

TABLE 39

Average Diet Intake and Excretion of Two Pig-tailed Monkeys (M. nemestrina) on Dry Purina Chow (4.1 kcal/g) Over a Period of 5 Weeks. (1)

	Number of Observations	Mean	Range
Calorie Intake (kcal/day)	70	757	742-761
Fluid Intake (ml/day)	70	770	577-900
Feces Production (g/day)	70	55.7	47.8-65.8
Urine Production (ml/day)	70	525	332-745

Note: Average body weights before and after the experiment period were 10.52 and 10.69 kg respectively.

TABLE 40

Average Diet Intake and Excretion of Two Pig-tailed Monkeys (M. nemestrina) on Nutrament(R) (1.08 kcal/ml) Over a Period of 17 Weeks. (1)

	Number of Observations	Mean	Range
Caloric Intake (kcal/day)	126	743	445-800
Fluid Intake (ml/day)	126	720	412-740
Feces Production (g/day)	126	39	18-66
Urine Production (ml/day)	126	280	165-338

Note: Average body weights before and after the experiment period were 6.20 and 7.22 kg respectively.

TABLE 41

Average Diet Intake and Excretion of Two Pig-tailed Monkeys (M. nemestrina) on Enfamil(R) with Iron (1.35 kcal/ml) Over a Period of 17 Weeks. (1)

	Number of Observations	Mean	Range
Caloric Intake (kcal/day)	126	673	485-780
Fluid Intake (ml/day)	126	501	359-577
Feces Production (g/day)	126	32	17-44
Urine Production (ml/day)	126	182	102-298

Note: Average body weights before and after the experiment period were 6.55 and 7.46 kg respectively.

TABLE 42

Degree of Acceptability of Various Natural, Raw Foodstuffs to the Pig-tailed Monkey (M. nemestrina). (11)

	Fruits	Leaves and roots	Seeds and nuts	Animal products	Juices, liquids or emulsions
EXCELLENT	Apples Apricots Avocadoes Bananas Casaba Cantaloupe Cucumbers Dates Dried apricots Dried peaches Oranges Peaches Tomatoes Watermelon		Corn on the cob Walnuts(in shell)	Larvae(meal worms,etc.) Quail eggs	Apple juice Buttermilk Cranberry juice Grape juice Milk Most fruit juices, raw or pasteurized Nut emulsions in water Whole egg emulsion in water, juice, or milk
GOOD	Egg plant Papayas Pineapple	Bell peppers Brussels sprouts Lettuce Mustard Greens Rhubarb Sweet potatoes Yams	Almonds(in shell)	Cottage cheese	

TABLE 42 (continued)

	Fruits	Leaves and roots	Seeds and nuts	Animal products	Juices, liquids or emulsions
VERY VARIABLE		Carrots Cauliflower Celery Diakon Parsnips Peas, edible-podded Peas, green Potatoes Turnip	Pecans Shelled almonds Shelled walnuts Sunflower seeds		
NONE		Mushrooms Seaweed, dry		Beef, chicken, & rodent raw livers raw hearts raw kidneys raw muscle Crab Dried crab Dried oyster Dried shrimp Fermented cheeses Earthworms Miscellaneous large fish cuts Oysters Shrimp	

TABLE 43

Composition of EPL D_{52} Diet with Preliminary Excreta and Hematological Data on 6 Pig-tailed Monkeys (M. nemestrina). (1)

Daily Intake (in two separate feedings).

Food Energy	686 kcal
Protein	30 g
Fat	19 g
Water	784 ml
CHO	100 g
Ash	5 g
Calcium	443 mg
Phosphorous	670 mg
Iron	7.1 mg
Sodium	424 mg
Potassium	6.5 mg
Vitamin A	15,115 IU
Thiamine	0.4 mg
Riboflavine	1.7 mg
Niacin	4.9 mg
Ascorbic Acid	68 mg

Urine Production: 500 - 600 ml/day

Urine pH: 5.5 - 6.7

Urine Specific Gravity: 1.007 - 1.014

Feces Production: 10-30 g/day

Hemoglobin: 10.4 - 13.5 g/100 ml

Red Blood Cell Count: 6.00 - 6.85 x $10^6/mm^3$

Hematocrit: 46 - 48

TABLE 44

Daily Body Temperature (^{0}C) of a Pig-tailed Monkey (M. nemestrina) Measured by a Thermistor Rectal Probe during Couch Restraint. (1)

Time	Number of Observations	Mean	Range
0100	5	39.0	38.3-39.5
0200	5	38.9	38.2-39.4
0300	5	38.9	38.4-39.2
0400	5	38.8	38.4-39.2
0500	5	38.8	38.3-39.1
0600	5	38.7	38.3-39.1
0700	6	38.6	38.3-39.0
0800	7	38.5	38.2-39.0
0900	7	38.6	38.2-38.9
1000	7	38.7	38.2-39.1
1100	6	38.7	38.3-39.2
1200	6	38.8	38.2-39.3
1300	6	38.8	38.2-39.3
1400	7	39.0	38.2-39.4
1500	6	39.1	38.4-39.6
1600	6	39.4	38.6-39.6
1700	7	39.6	38.6-40.4
1800	6	39.4	38.6-39.7
1900	6	39.4	38.5-39.7
2000	5	39.3	38.5-39.6
2100	5	39.3	38.4-39.6
2200	5	39.1	38.3-39.5
2300	5	39.1	38.4-39.6
2400	5	39.1	38.3-39.6

TABLE 45

Daily Body Temperature (^{0}C) Telemetered from an Implanted Transmitter in the Abdominal Cavity of a Caged Pig-tailed Monkey (M. nemestrina).(1)

Time	Number of Observations	Mean	Range
0100	150	35,7	35.2-36.5
0200	151	35.8	35.3-36.3
0300	153	35.8	35.3-36.6
0400	150	35.8	35.4-36.5
0500	141	35.9	35.6-36.6
0600	97	36.1	35.6-37.0
0700	65	36.7	36.0-37.6
0800	59	37.0	36.4-37.7
0900	385	37.1	36.4-37.8
1000	27	37.2	36.4-38.1
1100	30	37.3	36.6-38.1
1200	48	37.3	36.4-38.5
1300	47	37.3	36.6-38.2
1400	39	37.2	36.6-38.3
1500	36	37.3	36.8-38.0
1600	42	37.4	36.9-38.2
1700	59	37.4	36.9-38.2
1800	105	37.2	36.6-38.0
1900	129	36.9	36.2-38.0
2000	129	36.5	35.7-37.8
2100	134	36.1	35.4-37.1
2200	132	36.0	35.4-36.7
2300	130	35.9	35.3-36.6
2400	144	35.8	35.2-36.5

TABLE 46

Daily Body Temperatures (^{0}C) Telemetered from an Implanted Transmitter in the Abdominal Cavity of a Pig-tailed Monkey (M. nemestrina) under Two Different Light Conditions. (1,16)

	From 1 Feb to 19 Feb 1968 12 Hours Light:12 Hours Dark				From 20 Feb to 3 Jun 1968 24 Hours Light: 0 Hours Dark			
Hour	No. of Observations	Mean	Range Low	High	No. of Observations	Mean	Range Low	High
0100	19	35.7	35.4	35.9	88	36.4	35.6	37.0
0200	19	35.7	35.4	36.0	92	36.3	35.6	37.0
0300	19	35.7	35.5	36.1	89	36.4	35.5	37.0
0400	19	35.8	35.5	36.2	90	36.4	35.7	37.0
0500	18	36.0	35.6	36.3	88	36.4	35.8	37.1
0600	18	36.3	35.9	36.8	86	36.5	36.0	37.5
0700	17	36.9	36.7	37.3	84	36.8	36.2	38.2
0800	17	37.1	36.7	37.3	75	37.4	36.2	38.7
0900	15	37.2	37.0	37.4	64	37.8	36.7	39.0
1000	10	37.4	37.1	37.8	67	37.9	37.0	38.9
1100	11	37.5	37.2	38.0	63	38.0	37.1	38.8
1200	14	37.3	36.6	37.8	57	38.0	37.1	39.1
1300	13	37.5	36.7	37.9	65	37.8	36.9	38.6
1400	10	37.4	36.8	37.7	69	37.9	36.7	39.0
1500	11	37.3	36.6	37.8	68	37.9	36.7	39.0
1600	7	37.4	36.8	37.6	71	38.0	36.7	39.2
1700	8	37.5	37.2	37.8	71	37.9	36.7	38.4
1800	14	37.4	36.5	37.7	76	37.8	37.3	38.4
1900	19	37.0	36.2	37.3	74	37.8	36.8	38.8
2000	19	36.5	35.9	36.8	76	37.6	36.5	38.2
2100	19	36.1	35.8	36.5	77	37.3	36.7	38.0
2200	19	35.9	35.6	36.5	80	37.0	36.2	37.7
2300	19	35.8	35.5	36.2	78	36.7	35.7	37.5
2400	19	35.7	35.3	36.0	86	36.5	35.7	37.2

The thermal comfort zone of the pit-tailed monkey is a critical area which is as yet undefined. Listed below are some temperature characteristics of the closely related rhesus monkey.

TABLE 47

Temperature Characteristics of the Rhesus Monkey (M. mulatta). (17)

Rectal Temperature			Critical Air Temperature		Thermo-neutrality Zone
Normal °C	Min. °C	Max. °C	Low °C	High °C	
37-39	19	43	-	40	27-30

Critical Air Temperature: air temperature at which the normal animal first begins to show a change in deep body temperature.

Thermoneutrality Zone: the range of air temperatures at which the normal animal has the lowest metabolic rate.

Temperature Measured	Tolerance Limit			
	Extreme	Temperature °C	Duration	Survival n/n'
Air	Low	-20	2 hours	11/11

Average fall in rectal temperature was 3 °C.

TABLE 48

Body Composition Measurements on Pig-tailed Monkeys (M. nemestrina). (1)

	Number of Animals	Mean	Range	Method
Total Body Weight (kg)	63	6.07	4.00-10.00	
Total Body Water (ml/kg BW)	55	686	600-728	$^{3}H_2O$ dilution
Total Solids (g/kg BW)	55	315	272-400	BS=BW-TBW
Body Fat (g/kg BW)	55	63	5-165	$\%\ Fat=100-(\frac{\%TBW}{0.732})$
Lean Body Mass (g/kg BW)	55	937	835-995	LBM=BW-Fat
Extracellular Water (ml/kg BW)	56	260	200-352	^{14}C-Sucrose dilution
Intracellular Water (ml/kg BW)	50	446	377-512	$ICW=\frac{0.9(meqK)}{157\ meqK/liters}$
Total Body Potassium (meq/kg BW)	50	78	65-88	Whole Body Counting
Plasma Volume (ml/kg BW)	34	41	28-64	T-1824 dye dilution
Red Blood Cell Volume (ml/kg BW)	34	18	11-30	^{51}Cr-RBC dilution
Blood Volume (ml/kg BW)	34	59	46-83	BV=PV+RBCV

TABLE 49

Blood Volume Changes in 8 Pig-tailed Monkeys (M. Nemestrina) During 30-180 Days of Exposure to an Altitude of 3,800 Meters (474 torr Ambient Air Pressure). (1)

	Sea Level			3,800 Meters		
	Number of Observations	Mean	Range	Number of Observations	Mean	Range
Red Blood Cell Volume (ml/kg BW)	32	17.9	14.2-24.8	8	29.3	22.5-45.6
Plasma Volume (ml/kg BW)	32	28.2	21.7-39.7	8	24.4	19.2-29.9
Blood Volume (ml/kg BW)	32	46.1	38.4-64.5	8	55.2	47.5-77.1
Whole Body Hematocrit (%)	32	38.9	33.6-46.2	8	53.7	48.7-59.5

TABLE 50

Bone Density Changes in Pig-tailed Monkeys (M. nemestrina) on Two Types of Diets During Restraint and Non-restraint for a Period of 5 Weeks.(18)

Anatomic Sites	Basic Group* (no changes)	Bone Mass Changes with Changed Diet (Unrestrained Primates fed Diet B)	Bone Mass Changes in Basic Group Placed in Restraint (Restrained Primates fed Diet A)	Bone Mass Changes in Group with Changed Diet Placed in Restraint (Restrained Primates fed Diet B)
1. Skull	X	Bone mass increased ($P < 0.01$)	Mean loss of 5.6 percent during restraint	Mean loss of 4.7 percent during restraint Difference between groups N.S.**
2. Cervical Vertebra 1	X	Bone mass slightly increased ($P < 0.10$)	Mean loss of 8.5 percent during restraint	Mean loss of 3.7 percent during restraint ($P < 0.05$) Difference between groups significant
3. Cervical Vertebra 2	X	Bone mass slightly increased ($P < 0.10$)	Mean loss of 6.0 percent during restraint	Mean loss of 5.1 percent during restraint Difference between groups N.S.
4. Lumbar Vertebra 3	X	Bone mass markedly increased ($P < 0.01$)	Mean loss of 20.0 percent during restraint	Mean loss of 19.9 percent during restraint Difference between groups N.S.
5. Lumbar Vertebra 4	X	Bone mass markedly increased ($P < 0.01$)	Mean loss of 18.0 percent during restraint	Mean loss of 12.4 percent during restraint Difference between groups significant ($P < 0.05$)
6. Hand Phalanx 5-2	X	Difference between dietary groups N.S.**	Mean loss of 6.8 percent during restraint	Mean loss of 10.3 percent during restraint Difference between groups N.S.
7. Capitate	X	Bone mass slightly increased ($P < 0.10$)	Mean loss of 3.8 percent between tests	Mean loss of 0.7 percent during restraint Difference between groups N.S.
8. Distal Radius	X	Difference between dietary groups N.S.	Mean loss of 3.2 percent during restraint	Mean loss of 5.0 percent during restraint Difference between groups N.S.
9. Radius Diaphysis	X	Difference between dietary groups N.S.	Mean loss of 3.2 percent during restraint	Mean loss of 4.1 percent during restraint Difference between groups N.S.
10. Ulna Diaphysis	X	Difference between dietary groups N.S.	Mean loss of 8.6 percent during restraint	Mean loss of 8.3 percent during restraint Difference between groups N.S.
11. Olecranon	X	Difference between dietary groups N.S.	Mean loss of 10.3 percent during restraint	Mean loss of 1.6 percent during restraint Difference between groups significant ($P < 0.05$)
12. Medial Humeral Epicondyle	X	Difference between dietary groups N.S.	Mean loss of 6.3 percent during restraint	Mean loss of 6.0 percent during restraint Difference between groups N.S.
13. Femur Diaphysis	X	Bone mass increased ($P < 0.05$)	Mean loss of 14.0 percent during restraint	Mean loss of 10.3 percent during restraint Difference between groups N.S.
14. Patella	X	Bone mass slightly increased ($P < 0.10$)	Mean loss of 14.7 percent during restraint	Mean loss of 13.9 percent during restraint Difference between groups N.S.
15. Proximal Tibia	X	Bone mass increased ($P < 0.10$)	Mean loss of 14.8 percent during restraint	Mean loss of 10.5 percent during restraint Difference between groups N.S.
16. Tibia Diaphysis	X	Bone mass increased ($P < 0.01$)	Mean loss of 18.9 percent during restraint	Mean loss of 16.7 percent during restraint Difference between groups N.S.
17. Os Calcis	X	Bone mass slightly increased ($P < 0.10$)	Mean loss of 21.1 percent during restraint	Mean loss of 17.9 percent during restraint Difference between groups N.S.

*The Basic Group consists of Unrestrained Primates fed Diet A

**N.S. means "not statistically significant"

TABLE 51. Electroencephalographic Recording During Acceleration in the Pig-tailed Monkey *(M. nemestrina)*. (19)

Axis of Acceleration	G Loading	Exposure Time	Behavior of Subject	Brain Region	Electroencephalogram Characteristics
Vibration of whole body in three planes	0.25-in. double amplitude 5-10 cycles/sec, then 2-4 G peak to peak 5-40 cycles/sec	Spectral runs 5-40 cycles/sec for 10 min		Visual cortex, hippocampal system, amygdala, midbrain reticular formation, centrum medianum	"Driving" of electroencephalogram at shaking frequency in range 9-15 cycles/sec. Effect abolished by anesthesia, and dissociated in simultaneous records from adjacent structures and symmetric placements. "Driving" at half-shaking frequency in range 15-25 cycles/sec.
Transverse, (ventro-dorsal, eyeballs in)	8-10	3 min	Alert, at least up to 8 G	Visual cortex, hippocampus, amygdala, midbrain reticular formation	Visual cortex: initially much low-voltage fast activity, but interspersed with paroxysms of 1-5 cycles/sec high-amplitude slow waves at peak G. Hippocampus, amygdala, mid-brain reticular formation: wide spectrum of high-amplitude 3-9 cycles/sec activity, trending to slower dominants at peak G.
Transverse, in booster profile	10		Effects in "coast" phase after booster	Visual cortex, hippocampus, amygdala, midbrain reticular formation	Paroxysms of 2-3 cycles/sec high-amplitude slow waves lasting 5-10 sec. Missed beats and irregular rhythm in electrocardiogram occur consistently during these paroxysms and not at other times.
Longitudinal (head to tail)	7-8		Blackout at 8 G sustained 45-90 sec	Visual cortex, hippocampus, amygdala	In progression to blackout, visual cortical record slows and flattens first, followed by amygdala; only partial flattening in hippocampus record may occur.
			Recovery from blackout may be associated with jerking of limbs	Visual cortex, hippocampus, amygdala	Seizure-like spikes first in hippocampus, then in visual cortex, followed by amygdala.

TABLE 52

Measurement of Epididymal Sperm from 2 Pig-tailed Monkeys (M. nemestrina). (1)

	Mean	Range
Head Length (μ)	6.6	5.9-7.4
Head Width at		
Widest portion of anterior cap (μ)	4.3	3.4-5.3
Distal perimeter of cap (μ)	3.4	2.8-4.3
Base of head (μ)	2.2	1.6-2.8
Length of Mid Piece (μ)	10.8	9.4-13.3
Length of Tail (μ)	58.8	52.4-62.8

TABLE 53

Morphologic Characteristics and Biochemical Content of Semen from the Pig-tailed Monkey (M.nemestrina). (20)

	Number of Animals	Mean	Range
Volume (ml)	5	1.2	0.9-1.5
pH	5	7.5	7.2-7.8
Sperm Count ($x10^6$/ml)	5	5.9	2.0-9.7
Motility (% Progressive)	5	67	54-82
% Live	5	68	55-86
Fructose (mg/100 ml)	5	446	371-547
Lactic Acid (mg/100 ml)	5	64.5	45.2-108.7
Citric Acid (mg/100 ml)	5	115.3	58.5-173.7

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SECTION III.

REPORT OF THE APRL NUTRIENT SUBSYSTEM WORKING GROUP

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NUTRITION

Historical Perspective. Since July 1962, a number of dried, commercially prepared, pelletized foods have been used as a source of nutrients for monkey consumption. Purina Monkey Chow, as judged by its acceptability, availability, uniformity and ease of clean up in individual monkey cages has been used as a principal source. Other commercial diets, i.e. Wayne, CIBA, etc., have been tried in the cage and restrained conditions and found lacking in some respects when compared to Purina Monkey Chow. The main drawback in these diets has been in the area of acceptability. Two hundred grams of Purina Monkey Chow with water *ad libitum* and a 25 mg ascorbic acid tablet per day appeared to be adequate for a mature monkey, but not the optimum diet for critical physiological trials. For additional information concerning feeding in the early stages of the project refer to page 126 of "Handling Procedures and Equipment for Physiological Studies on the Pig-tailed Monkey *(Macaca nemestrina)*.[1]

Realizing that a fluid diet could provide a medium whereby the measurement of required nutrients can be made with precision, studies regarding the adequacy of such diets were initiated. Two commercially available fluid diets, Vanilla Nutriment and Enfamil with Iron, were shown to be adequate for a period of 126 days when provided as a sole source of nutrients and water[2].

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[1] Rahlmann, D. F., et al. Handling procedures and equipment for physiological studies on the pig-tailed monkey *(Macaca nemestrina)*. Lab. Animal Care, 14: 125-130, 1964.

[2] Rahlmann, D. F., et al. Adequacy of liquid diets for maintenance of pig-tailed monkeys. Lab. Animal Care, 18: 631-636, 1968.

A chemically defined diet (PD5), manufactured by Schwarz Bioresearch, with adequate water added was poorly accepted by the pig-tailed monkey until supplemental apple juice was added. An analysis of the feces and urine collected during the trial is currently in progress. Most of the time the feces were very soft, often to the point of being liquid and therefore difficult to handle.

Since July 1969 various trials have been conducted to develop our own fluid diets. Part of this research included a careful study of acceptance and effect of various natural foodstuffs[3].

During the past months our work has been revolving around homogenized diets prepared from natural foodstuffs using a Rietz Disintegrator.[4]

As expected, the monkeys accepted these natural diets much more readily. Their desire for them, after many months, never varied, as it did when other types of fluid diets were fed. These other diets were based on or contained purified or synthetic ingredients. There is no need to stress the importance of this continuous and prolonged acceptance.

The greatest obstacle in formulating a proper diet was to keep the urinary pH on the acid side, while having a nutritionally balanced diet. This problem seems now solved with a diet called "D52", which is fed twice daily.

APRL Proposed Experimental Procedure. A homogenized diet similar to D52 will be fed to each animal every 12 hours through a properly fitted tube that will release the fluid when touched by the tongue

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[3] Spiller, G. A. and Rahlmann, D. F. Physiological effect and acceptance of various natural foodstuffs in the pig-tailed monkey *(Macaca nemestrina)*. Lab. Animal Care, 20: 494-498, 1970.

[4] Rietz Manufacturing Co., Santa Rosa, California.

of the monkey. This fluid will supply all the nutrient and the water needed, so no separate water will be fed.

The food will be stored in:

Choice one: A single aseptic reservoir

Choice two: can-like containers containing the daily ration

The choice depends on the current work on the preservation of the homogenate. The diet formula is given in Table 1, and the approximate nutrient content in Table 2. Amounts and some characteristics of urine and feces are given in Table 3 together with mean hematological values for six monkeys on D52.

The feces have a good consistency that will allow proper handling of them in the spacecraft. Proper collection of urine and feces in the spacecraft will allow measurements of nutritional interest during and after the flight.

Current and Future Research On Homogenates. During the next few months the formula of D52 will be further tested and possibly modified, if necessary, to insure proper nutritional balance and maintenance of correct physiological parameters for prolonged periods. The correct caloric requirement on this type of homogenate is being carefully tested. The same tests will have to be repeated with animals under restraint first, and then with animals under restraint plus the various surgical procedures that will be performed on the space monkey.

Another essential facet of current work is the preservation of the diet for prolonged periods. Presently the diet is kept refrigerated until feeding time, and this way is kept in satisfactory condition for about 10 days.

The Department of Food Science and Technology of the University of California at Davis is currently working with us to develop an aseptic diet in an aseptic container (or containers). Nutritional values and stability of the homogenate might be influenced. Decreased microbial population and lower enzymatic content in the diet will certainly have a bearing on the physiology of digestion of the primate. All these facts remain to be studied in co-operation with the food technologists. Changes in formula might then be required.

Summary. A fluid homogenized diet based on natural disintegrated foodstuffs seems the best answer to prolonged and prompt acceptance. A homogenate makes possible the use of a *single container* and carefully controlled intake of food and water, with *minimum waste*. Water and nutrients ratio is the same each day of the flight. Feeding twice daily seems a necessity to guarantee a consistently acid urine.

Currently work is in progress to further test the nutritional values of the diet and to preserve it for prolonged periods of time. However, of all the various types of solid or fluid diets studied thus far, none seems to combine all the nutritional and technical advantages of this new homogenate of natural foods.

TABLE 1

Composition of Diet D52 Homogenate

Per Monkey Fed 900 ml per day

Apples	81.9 grams
Eggyolks	46.8 grams
Lettuce	18.7 grams
Cranberry juice	295.2 grams
Yams	18.7 grams
Cottage cheese	84.7 grams
Buttermilk	147.6 grams
Molasses	34.4 grams
Liver	26.0 grams
Water	186.8 grams

TABLE 2

Average Daily Intake of Nutrients for a 20-Pound Monkey Fed D52 with No Additional Water and in Two Separate Feedings

Food Energy	686 kcal
Protein	30 grams
Fat	19.7 grams
CHO	99.6 grams
Fiber	0.9 grams
Water	784 grams (mls)
Ash	4.7 grams
Calcium	443 mg
Phosphorus	670 mg
Iron	7.1 mg
Sodium	424 mg
Potassium	650.9 mg
Magnesium	125.3 mg
Vitamin A Value	15,115 I.U.
Thiamine	0.4 mg
Riboflavin	1.8 mg
Niacin	4.9 mg
Ascorbic Acid	67.7 mg
Cholesterol	1304.3 mg

TABLE 3

Physiological Parameters for Monkeys Fed 900 ml of D52 Homogenate Per Day Without Additional Water

URINE PER 24 HOURS:	
Volume:	500 to 600 ml
Specific gravity:	1.007 to 1.014
pH:	5.5 to 6.7
FECES PER 24 HOURS:	
	10 to 30 grams
HEMATOLOGY:	
PCV (%):	46-48
RBC x $10^6/mm^3$:	6.0-6.8
Hemoglobin (gm%):	10.4-13.5
Mean Corpuscular Hemoglobin (μμg):	17.0-19.5
Mean Corpuscular Hemoglobin Concentration (%):	25.0-29.6

ENGINEERING

1. Introduction

This section presents an engineering discussion of the Phase I study of the Automated Nutrient Subsystem as it exists currently. Additions and deletions will be made as progress of the engineering-biology interface demands.

Study - Technical requirements will be derived from the scientific guidelines (including the completion of the T.B.D.'s) furnished by the Biologists. These data will be used for analyses and design to develop a configuration base line for the Automated Nutrient Subsystem concepts. Both single and multiple container approaches will be considered within the known state of the art fabrication techniques. Trade studies will be performed in collaboration with the scientific staff to ensure that the optimum base line concept for the time span alloted is chosen. Hardware that is already proven to be reliable will be used whenever possible.

Responsibility - The engineering systems integration will have over-all responsibility for integrity and engineering design.

Program Approach - The engineering approach to the Nutrient Subsystem will be to safeguard the quality of the nutrient and assure the presentation of the liquid diet when, where, and how it is specified by the Biologists. Of necessity, engineering development must be done on most components of this subsystem; however, the development of hardware is not the purpose of this program. It is the biological experiment support system that is most important and therefore its needs determine the guidelines.

2. Scientific and Technical Integration Plan - To attain the primary objectives of the Automated Nutrient Subsystem, a proposed operational plan has been considered. Two systems will be studied in parallel, a single container for the entire mission of 60 days or more and a daily ration system of 600 to 900 ml.

2.1 System Engineering and Integration - The integration of this particular subsystem is more of an engineering category than biological and hence will be coordinated closely with the data handling system when development begins. To ensure an acceptable system all preliminary studies will be done through close collaboration and coordination with the Nutrient Subsystem Committee. This document will contain all specific base line data for subsystem guidelines.

2.2 Reliability Analysis and Criteria - The reliability concepts will be blended with conceptual studies through close association of reliability and design concepts. As Phase II A progresses, a reliability value will evolve based upon trade studies and system development.

The design review activity will be continuous to assure a high reliability and confidence level in the final design. It also provides an opportunity to coordinate ideas between the engineering elements of the working team and provides the means for carrying our reliability disciplines into each design phase.

2.3 Task Description - Engineering will provide the support and services necessary to accomplish the following effort.

2.3.1 Liaison - Engineering will maintain a close technical liaison with the science coordinator to assure an optimization of the proposed items of work.

2.3.2 APRL Systems - To facilitate the analysis of the design concepts, it is necessary to consider all interfacing subsystems. Appropriate techniques will be used to ensure the orderly development of base line criteria and to study the interaction between the nutrient subsystem and other subsystems. Those subsystems having the closest interface are the Monkey Module, the Data Acquisition subsystems, and the Environmental Control Subsystem.

2.3.3 Technical Documentation and Reports - Documentation for this study effort will be provided to define a nutrient subsystem configuration base line design concept and performance criteria. Analysis summaries and configuration study drawings will be provided as appropriate, to substantiate and further define the concepts selected.

2.3.4 Master Schedule

2.4 Boundary Conditions and Constraints - The boundary conditions and the constraints that serve to direct the nutrient subsystem base line data include:

Amount of nutrient/day	700 to 900 ml
Storage temperature	18°C
Presentation temperature	23°C
Settling characteristics	TBD
Time of presentation: Twice daily	0600 to 0800 and 1600 to 1800 hours
Volume of presentation 0600 feeding 1800 feeding	 400 ml maximum 500 to 900 ml constituting balance in reservoir
Maximum daily volume	900 ml
Rate of presentation	1 ml/sec

Number of days of presentation:	
pre-mission	15
mission	60
post-mission	15

2.4.1 The Requirement for Scientific Validity of Data

T/M Bits/sec	TBD
No. of acceptances	TBD
Time of acceptances	TBD
Length of time of each acceptance	TBD
Volume of each acceptance	TBD
Total volume/day	TBD

The requirement for the scientific integrity of the complete subsystem.

The requirement for the Automated Nutrient Subsystem to operate automatically and continuously for 60 days, but with the capability for 90 days in the unattended mode.

The requirement for the subsystem to operate in a non-gravitational environment.

2.4.2 Functions - The various functions which will be performed to define the preliminary base line of the nutrient subsystem will be analytical, evaluative, and studied, in nature. These functions which will have T/M override capabilities, include:

The acquisition of information and data pertinent to design.

Assessment of the present state of the art hardware.

Trade study effort to determine an optimal design concept.

Evaluation of component suitability in terms of performance characteristics.

Evaluation of component suitability in terms of APRL requirements.

2.4.3 Products - The products include:

Presentation of nutrient subsystems design concept.

Definition of general engineering criteria essential for design of the Nutrient Subsystem.

Evaluation of the compatibility between the monkey/subsystem interface.

Evaluation of the compatibility between component-to-component interface, for component-to-subsystem interface, and for subsystem to APRL interface.

Circumscription of the major problem areas.

Identification of the high risk areas.

Definition of subsystem preliminary base line design.

3. Physiology/Engineering Interface - The APRL is an orbital laboratory for the study of environmental physiology. The research objective is the investigation of physiological effects of weightlessness.

3.1 The Automated Nutrient Subsystem - The term automated is meant to cover the chain reaction caused by the monkey sucking on the mouthpiece with a 10 torr (negative) force. This chain reaction occurs as follows:

1. Monkey sucks on mouthpiece →
2. Line pressure drops - 10 torr or more →
3. A bellows sensor is actuated by the pressure drop (however the food nutrient does not touch the bellows proper) →
4. The bellows closes an electrical circuit →
5. a) The circuit is energized or deenergized by a circuit programmer →
   The make or break of the circuit causes
   b) A counter to be activated to record the feeding frequency →
6. The circuit programmer contains a 24-hour clock to control the presentation time and limit it to 0600 to 0800 and 1600 to 1800 hours →

7. The circuit, if energized between the proper pre-set presentation hours will activate a flow valve →

8. The flow valve opens upon signal starting at -10 torr and from that point on, increase the volume in proportion to increase in negative pressure with a lag in cut off point to approximate -5 torr. This allows liquid nutrient to move from the reservoir to the mouth piece →

9. The movement of the nutrient activates a flow sensor →

10. The flow sensor is T/M or hard wired to a recorder for noting increment volume and/or total volume of nutrient expelled through the mouth piece.

11. The design configuration of the reservoir and mouthpiece has not been rigidly decided at this writing.

12. Non-wetting materials are to be considered in all areas.

13. The rate of flow will be metered to 1 ml/sec out of the nipple orifice.

14. Temperature control will be considered for both storage and presentation.

15. The I.D. of the feeder line and mouthpiece tube will be dependent upon the flow and caking characteristics of the nutrient liquid.

SECTION IV.

REPORT OF THE APRL ENERGY METABOLISM SUBSYSTEM WORKING GROUP

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The primary purpose of this report is to summarize briefly the present state, within the Environmental Physiology Laboratory, of concept development and experimentation in the general area of energy metabolism, as related to the objectives of the APRL experiment. This critical review is intended to identify areas where either or both research and design concepts are lacking, and to establish priorities for future research and development.

APRL Proposed Experimental Procedure. According to the APRL experimental proposal, energy metabolism will be determined by indirect calorimetry utilizing a flow through, open-circuit system. In addition, the proposed design of the primate capsule will also allow for the calculation of energy expenditure through direct calorimetry, thus providing a cross-check for the indirect method.

For the indirect method, oxygen consumption, carbon dioxide production, and respiratory quotient will be calculated from the gas inlet and outlet partial pressures of O_2, CO_2, N_2, and H_2O, in addition to the gas inlet and outlet temperatures and the gas flow rate. The methods for calculating each of these variables have been outlined in section 3.3 of the document, APRL NUTRIENT AND METABOLIC GAS SENSING SUBSYSTEMS (EPL 67-2).

For the direct method, the radiant, conductive and convective heat loss rate, the evaporative water loss rate, and the animal's heat production will be determined from the differential between the inlet and outlet water jacket temperature, the inlet and outlet pH_2O, and the inlet and outlet gas temperatures.

Historical Perspective. To date, only limited research has been conducted in this laboratory concerned with the energy metabolism of primates. A total of 18 metabolic runs of varying durations were conducted on 4 pig-tailed monkeys between October, 1962 and March, 1964. The results of these runs have been summarized by Pace, et al.[1] An additional 3 runs of varying durations were conducted on 2 pig-tailed monkeys during the month of August, 1968. The data collected during these experiments are limited in scope and are somewhat questionable in accuracy and meaning.

Critical Review of the Proposed Experimental Procedure. The McDonnell Douglas Corporation, in the document APRL NUTRIENT AND METABOLIC GAS SENSING SUBSYSTEMS (EPL 67-2), report the results of an extensive review of the proposed metabolic subsystem. The main criticism identified in this document concerns the lack of suitable gas detecting systems or analyzers which have the required sensitivity and are, or could be in the near future, qualified for space flight. They feel that the degree of analysis sensitivity needed to satisfy the experimental requirements and specifications is not available in any of the present systems or analyzers. Section 3.3 of the document (EPL 67-2) illustrates the calculated magnitude of this problem.

In reviewing the previous literature concerned with metabolic assessment of primates and other animals of comparable size (see references for Table 1), it is quite clear that the proposed method should be applicable to the APRL experiment. The gas analysis

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[1] Pace, Nello, et al. Preliminary observations of some physiological characteristics of the pig-tailed monkey, *Macaca nemestrina*. Aerospace Med., 35: 118-121, 1964.

instrumentation used in these previous studies is similar in sensitivity to existing systems or analyzers which are close to being, or have been flight qualified.[2] However, it is obvious that many of the potential problems related to lack of gas analysis sensitivity would certainly be eliminated or reduced if consideration could be given to minimizing the dead space within the capsule.

It is obvious from the above that it is imperative that research begin at once to answer many of the unresolved problems in this area of energy metabolism. What is needed is a substantial and immediate effort in breadboarding the APRL concept in the Environmental Physiology Laboratory. Only then will it be possible to identify the actual problems associated with this method. It is highly possible that actual experimentation will lead to unpredictable modifications of the presently proposed system which will enhance the scientific validity and accuracy of this part of the total experiment.

Alternative Procedures. In the event that the presently proposed procedure proves unsatisfactory for one reason or another, the work group would suggest the following alternative approaches which might be adaptable to space flight.

a. Helmet or Hood -- By using a helmet or hood it is possible to obtain nearly a breath-by-breath analysis of the metabolic activity of the animal. The front section of the hood could be mobile and, therefore, the animal would have access to his face during those periods when measurements were not being made. This approach would be preferable if exercise

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[2] The mass spectrometer under development by NASA's MSC in Houston could well be the answer to this problem.

were to be included in the proposed experiment. The major weakness to this approach is the necessity of having two duplicate gas management systems, and the problems of detecting heat exchange and water loss from two separate chambers rather than just the one.

b. Tracheotomy -- This approach, likewise, gives breath-by-breath analysis accuracy. This would probably be the best way to evaluate the animal under conditions of exercise. However, there are many disadvantages to this procedure, including some very difficult interfacing problems and the additional surgical trauma.

Dynamic Range of Metabolic Variables. A thorough review of the research literature was undertaken to determine the variability in metabolic values under a variety of conditions for various primates. This data was then standardized to allow an interpolation of what might be expected of the pig-tailed monkey. Allowances must be made, however, for the differences in temperament, excitability, etc. between the various species. Using man as a model for estimating the metabolic cost of various activities, it is also possible to estimate the extreme dynamic ranges that might be experienced by the monkey. These data are presented in Tables 1 and 2.

Summary and Conclusions. The energy metabolism area seems to be lagging far behind all other areas involved in the overall APRL experiment at the present time. It is strongly reommended that priority be given to research and development in this area so that it will be at least

up to the level of the other areas within the next 6 months. Experimentation should begin immediately in this area even if it involves, because of inadequate instrumentation or equipment, only crude estimates of metabolic activity. Lastly, parallel efforts should be given towards developing either or both of the two alternative procedures. This would provide standby or fallback systems if needed, and could be used for the exercise metabolism studies once research activity begins in that area.

Table 1. Energy metabolism of primates under various conditions

Primate	Reference[1]	N	Conditions	Weight kg	Metabolic Rate kcal/day	SMR[2]	kcal/day/wt$^{3/4}$
Baboon	Savage	8	Anesthesia	15.85	611.6	555.8	77.03
	Savage	7	Anesthesia	16.32	640.5	568.4	78.88
	Bruhn	3	Sleep	5.3-7.6			76.52
Chimpanzee	Bruhn	3	Sleep	14.1-24.5			66.04
	Bruhn, Benedict	29	Basal	2.9-48.1			78.51
	Benedict	10	Basal	31.1-48.0			40.66
Gibbon	Bruhn	1	Sleep	1.9	132.2	113.4	81.63
Mangabey	Bruhn	2	Sleep	2.5-2.9			68.59
Orangutan	Bruhn	1	Sleep	16.2	586.6	565.6	70.37
Rhesus	Bruhn	3	Sleep	3.7-8.1			67.91
	Benedict	14	Basal	3.3-5.1			68.60
	Rakieten	11	Rest	2.7-3.7			64.77
	Karel	4	Anesthesia	3.3-3.6	(tracheotomy)		116.92
Pig-tailed	Pace	1	Sleep	10.0	513.6	393.4	91.40
		1	Rest	10.0	571.2		101.60
		1	Active	10.0	1468.8		261.30
Squirrel	Malinow	9	Rest	0.89	99.6	63.9	91.00

[1]References:

Benedict, Francis G. Vital Energetics: A Study in Comparative Basal Metabolism. Carnegie Institution of Washington, Washington, D. C., 1938.

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Rakieten, Nathan. The basal heat production of the rhesus monkey. J. Nutr., 10: 357-361, 1935.

(continued)

Table 1 (continued)

Savage, Nerina and B. W. Goldstone. Effect of different dietary fats on oxygen consumption and on serum lipid levels in the baboon. British J. Nutr., 19: 459-467, 1965.

[2]Standard Metabolic Rate: $70(Wt^{3/4})$

Table 2. Energy required by a 154-pound man for various physical activities and the interpolated equivalent for a pig-tailed monkey

Activity	MAN		MONKEY
	Total kcals per hour[1]	Increase above Basal Rate	Interpolated Equivalent (kcals/hr)
Sleeping (basal rate)	70	--	21.4
Lying quietly	80	1.1 x's	23.5
Sitting	100	1.4 x's	29.8
Standing	115	1.6 x's	34.2
Light calisthenics	170	2.4 x's	51.2
Walking, 2 mph	175	2.5 x's	53.4
Mountain climbing	600	8.6 x's	184.0
Long term maximal work	1400	20.0 x's	426.5
Short term maximal work	9000	128.5 x's	2743.0

[1]Adapted from: Morehouse, L. E. and A. T. Miller. Physiology of Exercise. 5th ed. St. Louis: C. V. Mosby Co., 1967. pp 190-191.

SECTION V

REPORT OF THE APRL HEMODYNAMICS SUBSYSTEM WORKING GROUP

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This report summarizes the hemodynamic data obtained from the pig-tailed monkey in the Environmental Physiology Laboratory to date. It identifies areas where additional hemodynamic base-line data are needed. It outlines the procedures that might be utilized in the APRL development. Finally, consideration is given to the implementation of the biology/engineering interface for the APRL hemodynamics subsystem.

Characteristics of the hemodynamic data.

Hemodynamic measurements from couch restrained monkeys made in conjunction with chronically implanted polyvinyl catheters are shown in Table 1. These measurements can be considered as those of a mature male pig-tailed monkey positioned relatively comfortably in a fiber glass couch, and further restrained with a plexiglass leg guard and nylon raschel net jacket with appropriate straps. In some cases a chest guard was placed across the monkey to prevent any attempt to handle exteriorized vascular catheters. The instrumented monkey was isolated from outside visual contact, and noise levels in the laboratory were fairly constant from day to day with the exception of the weekends. Daily light:dark cycles were maintained at a 12 hr:12 hr basis initiated at 0600 and 1800 hours respectively. In all cases,

as indicated by his feed and water consumption, the monkey could be considered as reasonably well adjusted to his environment.

Despite the attempt at environmental control, it is of interest to note some of the rather wide variation that occurs with the various hemodynamic measurements. Table 1A contains some earlier measurements of hemodynamic parameters when the subject monkeys, although unanesthetized, were maintained under somewhat less controlled environmental conditions. In general, blood pressures are similar to those reported for man but other parameters, such as heart rate, cardiac output, stroke volume, etc., can not be compared empirically. Physiologically, however, the mature pig-tailed male reacts identically to man when certain hormonal regulatory substances such as epinephrine or norepinephrine are intravascularly administered. The cardiovascular changes in the pig-tailed monkey infused with these substances are shown in Table 2. While the amount of the substance might be considered as unphysiological, comparative experiments with man have shown that epinephrine in both species causes an increase in heart rate, cardiac output, stroke volume, and cardiac work. Mean aortic pressure remained relatively the same while the rise in systolic pressure is associated with a small decline in diastolic pressure. Systemic resistance is also reduced. Norepinephrine decreased cardiac output and lowered heart rate to the extent that stroke volume is actually increased. Systolic, diastolic and mean aortic pressures were all increased. All of these shifts in hemodynamic parameters may be expected in the monkey as a result of a sudden change of external environment.

Another example of the possible changes in hemodynamics can be visualized from variations in body temperature. The effects of hypothermia or lowering of body temperature are shown in Table 3. Isoproterenol, a drug known to have a sympathomimetric effect on cardiovascular system, has also been used in this laboratory and the hemodynamic changes are shown in Table 4. Variations in hemodynamic measurements may also be expressed as a result of changes in ambient pressures. In order to detect these changes, pig-tailed monkeys have been exposed to the gaseous environments at the Barcroft Laboratory of the White Mountain Research Station and artificially reduced air pressures equivalent up to an altitude of 4,000 meters. The data shown in Tables 5 through 9 are representative of what may be experienced if a transient shift in ambient pressure occurs or a longer term lowering of pressure is maintained for periods of one to thirty days.

Eight adult male pig-tailed monkeys have been kept in the couch configuration for 90 days or longer. Four of these chronically intravascularly catheterized monkeys were undisturbed by other experimental impacts and cardiovascular measurements were made throughout the course of their confinement. Figure 1 shows the change in normalized cardiac output information. On the basis of this information one may expect hemodynamic measurements to vary considerably during the first month of confinement and tend to approach a more stable condition thereafter.

Varying amounts of arterial blood have been withdrawn and returned to the animal during the course of our experimentation with the dye dilution method for the determination of cardiac output in the pig-tailed monkey. Less than 2.5% of the whole blood volume is removed and returned during one of these cycles. Table 10 shows some data recorded on the

cardiovascular system while varying amounts of blood were being withdrawn and subsequently returned to the animal. The maximum amount of blood withdrawal was equivalent to approximately 5% of the animal's total blood volume, or twice that required for routine cardiac output determination. As noted, no major changes were seen in heart rate and aortic systolic and diastolic pressures.

For additional determination of base line hemodynamic parameters, flow probes have been chronically implanted in conjunction with vascular catheters. If the instruments are accurately calibrated before implantation, a reasonable estimate of flow rate can be determined from heart beat to heart beat without the injection of an indicator dye. Flow probes, once implanted within the animal body, are difficult to check for accuracy although electronic calibrations of the exteriorized equipment can be made. Tables 11 and 12 show the comparison of blood flow rates as recorded by an electromagnetic flow meter and cardiac output determined by dye dilution. In one case (Table 11) the pre-implantation calibration of the flow probe was considered to be more precise than the calibration of the instrument placed in the animal referred to in Table 12. The difference is considerably decreased when care is taken to perform an adequate calibration.

The advantages afforded by exteriorized chronically implanted vascular catheters are not limited to an application of a proven means of cardiac output determination. After a thorough study of biologically acceptable materials, the choice of polyvinyl chloride (PVC) tubing (Surprenant) over silastic, polyethylene, polypropylene, teflon, Kel F or polyvinyl chloride treated heparin adsorbed graphite has proven to be the most satisfactory for overall consideration in measurement of cardiovascular

data. Sensors can be arrayed outside this catheter material for the determination of pertinent aspects of blood condition related to hemodynamic changes. The development of a densitometer utilizing the catheter as a cuvette allows blood to be withdrawn without the need of extraneous connectors or sharp bends which may form a convenient place for the start of blood coagulation. A comparison of cardiac output as determined with catheter cuvette and the Gilford densitometer is shown in Table 13.

By continuing blood withdrawal beyond the outlining of the initial dye dilution curve, plasma dye clearance can be determined and, with extrapolation back to the time of dye injection or zero time, total blood volume can be calculated. Total blood volumes determined by this technique are shown in Table 14. The values obtained compare favorably with whole blood volumes obtained by the conventional methods employing T-1824 dye and 51-chromate labelled red cells (Table 15).

Preliminary studies have indicated that a measurement of the refractive index or the critical angle of reflection of the plasma interface between the inside catheter wall and the moving mass of red cells can be correlated to the amount of plasma protein in the blood. The amounts of total and various individual plasma proteins of the male pig-tailed monkey have been determined in this laboratory and are shown in Table 16.

Blood gas analyses using the Van Slyke apparatus and the Radiometer in addition to the physical aspects of respiratory gas exchange have been studied to some extent in this laboratory. Ventilatory and related blood chemical base line data from a restrained pig-tailed monkey

breathing room air are shown in Tables 17 and 17A. Blood gas analysis of samples taken from chronically implanted vascular catheters of 6 adult male pig-tailed monkeys is shown in Table 18. The oxygen hemoglobin dissociation curve relating oxygen carrying power of the blood for the male pig-tailed monkey has also been determined and the results are indicated in Table 19. In contrast to serial sampling of blood, a miniaturized Clark type polarographic electrode has been used to make continuous oxygen partial pressure measurements directly in blood vessels located on the right and left sides of the cardiovascular system. An example of data obtained from a couch restrained unanesthetized monkey with the probe surgically implanted in the aorta via the left subclavian artery is shown in Table 20. During this trial the monkey was maintained within an altitude chamber and the ambient air pressure was varied from an equivalent of sea level to 3800 meters.

The effects of accelerative forces on the hemodynamic system must be considered in relationship to the fulfillment of the APRL experiment. In Table 21 the dynamic ranges of heart rate, aortic and pulmonary arterial blood pressures are presented. An upper limit of 12 *g* was used as this force is the maximum which may be experienced during a Thor Augmented Delta launch profile.

Exercise.

Little work has been accomplished in this laboratory concerning the area of exercise as it relates to the APRL experiment. Consideration should be given to exercise as either a preventive measure, i.e., preventing cardiovascular deconditioning, or as a means of assessing cardiovascular and general deconditioning. If exercise is used as a

preventive measure, it is suggested that more than one animal be considered for flight, e.g., four animals in flight simultaneously with only two undergoing a routine exercise program. If exercise is to be used to assess cardiovascular and general deconditioning, then serious consideration should be given to the level, duration, and frequency of the exercise. The latter is a necessity as the test itself could be enough of a cardiovascular stimulus to prevent or reduce the magnitude of the animal's true adaptation to extended periods of weightlessness.

AREAS OF CONCERN IN AUTOMATED CONTINUOUS HEMODYNAMIC MEASUREMENT

Catheter Patency

It is anticipated that when direct blood pressures and cardiac outputs are determined on a daily basis on a monkey, comfortably couch restrained, that patency can be maintained for periods in excess of 120 days. This allowance is also made with the understanding that the automatic blood withdrawal system will provide adequate flushing without heparinization of the experimental animal. As mentioned previously, polyvinyl chloride catheters offer advantages over other types of plastic material.

Blood Pressures

A "dead ended" system for blood pressure measurement will not be satisfactory on any catheter through which blood must be withdrawn and returned for the determinations of hemoglobin, plasma proteins or cardiac output. In order to reduce the number of connections and eliminate extensive valving we have extended investigation on the use of a flow-through transducer. A system which utilizes a small thin-wall bubble

within the catheter in conjunction with a modified plastic dome, and Statham strain gauge transducer has been shown to produce identical blood pressure wave forms as those obtained with more conventional methods. Some additional work is needed to perfect this system, particularly with problems of drift from zero base line, hysteresis and adequate flushing within the "bubble" portion of the catheter.

Calibration of the instruments for pressure measurement up to the present have been accomplished by disconnecting the fluid filled line or with a valve bypass. An appropriate method for pressure transducer calibration must be developed to accomplish this task by automatic programming or on demand without manual interference.

Proper positioning of the pressure transducers should be maintained to minimize distortion artifacts caused by alterations in gravitational forces during the launch and recovery phases.

Cardiac Output

a) Dye injection. To maintain accuracy of the dye dilution technique, the precise amount of dye solution injected into the venous side of the heart must be known. We can be reasonably assured that if light does not enter the dye solution reservoir, no deterioration will occur and the dye concentration will remain stable. However, for the length of the test period as planned in APRL, greater assurance would be a necessity. Therefore, a calibration sensor to detect changes in dye concentration will be needed. The dye delivery system presently in use will inject accurate amounts of fluid in terms of volume, but does not include a sensor to accurately measure dye concentration.

b) Blood withdrawal, return, and catheter flushing.

The present syringe has been tested for continuous use in conjunction with a vascular catheterized monkey for periods up to 72 hours. Blood withdrawal and return appear to be adequate with no apparent hematological damage. The heparin saline flushing sequence following the return phase is not satisfactory. Blood is insufficiently cleared from areas within the proximal portion of the catheter and blood tends to flow slowly from the animal back into the catheter. This area then becomes a potential source of blood coagulation. Undoubtedly a considerable amount of work must be done to correct this situation for prolonged automated physiological measurement.

Practically all of our trials have been concerned with blood withdrawal from the aortic catheter. If hemoglobin and oxyhemoglobin levels are also to be determined in pulmonary arterial blood, some consideration must be given to the problems involved with a syringe connected to this respective vascular catheter. With regard to other implanted catheters not requiring blood withdrawal, provision for intermittent flushing must be made to prevent potential damping of pulse wave forms.

Electrocardiogram

While the electrocardiographic techniques used in this laboratory have provided excellent recordings, they are not functional for more than a 15-20 day period. The design and development of electrodes for long-term application should not present any major problems due to the current state of the art. It is recommended that attention be given to the development of such a system and to include experimentation to determine if satisfactory performance can be obtained over a 90-120 day period.

It is also suggested that consideration be given to implantable telemetry. This would greatly simplify many of the present problems associated with hard-wire electrocardiography, as well as reduce the number of cables, or wires hanging from the monkey.

Heart Rate

This measurement presents no immediate problem as it is contingent with the wave forms presented from the pressure transducers or the electrocardiographic sensors.

Respiratory Rate

Providing venous pulse recordings are adequate, the respiratory rate can be determined from this measurement. If not, alternative methods, for example a pneumotachograph, or appropriately positioned EKG sensors on the body surface or surgically implanted for telemetry transmission, may serve this purpose.

Blood Gas Analysis

In addition to the measurement of systemic and pulmonary oxygen saturation by densitometry, an implantable Clark type polarographic electrode for the continuous measurement of the partial pressure of oxygen has been tested in vivo with the male pig-tailed monkey. This instrument has remained functional for periods up to 90 days. Performance has been somewhat erratic and to be properly calibrated within the animal body a vascular catheter must be surgically placed within close proximity, particularly on the venous side. At the present time it is reasonable to assume that the electrode can perform satisfactorily over a prolonged period in the animal body, provided the subject is not traumatized by extensive additional surgical implants.

Some consideration has been given to the fabrication and implantation of an electrode capable of measuring the partial pressure of carbon dioxide in the bloodstream. The electrode would sense pH changes in the blood which can be correlated to the carbon dioxide content. One of the problems has been that miniaturization of pH electrodes are associated with increased impedance. If an electrode can be fabricated to the size of about 0.5 mm in diameter with an impedance not to exceed 10^{12} ohms, the continuous measurement of blood carbon dioxide may be feasible.

Temperature of Blood Vessel Walls

Initially, it was proposed to measure the temperature of the blood directly in vascular bed. By using two thermocouples, one within the bloodstream and the other placed appositionally but on the outer blood vessel wall, a small difference of 0.1°C was noticed. However, this was deemed insignificant when compared to the added problems of maintaining a sensor within a blood vessel.

Table 1. Hemodynamic measurements of 16 mature male pig-tailed monkeys.

Measurement	No. of Measurements Included in Mean	Mean	Standard Dev	Range Low	Range High
Body Weight (kg)		8.04	1.21	6.50	9.89
Respiratory Rate (breaths/min)	756	34	6	23	44
Heart Rate (beats/min)	756	193	16	168	223
Aortic Systolic Pressure (torr)	748	127	15	104	166
Aortic Diastolic Pressure (torr)	748	76	9	55	90
Aortic Pulse Pressure (torr)	748	51	11	37	68
Aortic Mean Pressure (torr)	756	100	11	83	115
Venous Mean Pressure (torr)	550	-0.6	1.4	-2.3	+ 2
Left Atrial Mean Pressure (torr)	208	-0.9	1.2	-2.9	0.7
Pulmonary Arterial Mean Pressure (torr)	74	16.5	3.5	13.0	23.5
Cardiac Output	378				
ml/min		968	248	623	1,437
ml/kg/min		122	23	90	171
Stroke Volume (ml)	378	5.4	1.3	3.1	12.0
Systemic Resistance (dyne sec/cm^5)	378	8,505	2,210	6,304	12,416
Left Ventricular Power (watts)	378	.216	.069	.118	.351
Pulmonary Resistance (dyne sec/cm^5)	74	1,313	578	835	2,404
Right Ventricular Power (watts)	74	.039	.011	.021	.054

Table 1A. Range in Hemodynamic Data from 5 Unanesthetized, Male Pig-Tailed Monkeys Weighing between 7.5 and 11.0 kg

	No. of Observations	Maximum	Minimum
Respiratory Rate (breaths/min)	97	42	20
Heart Rate (beats/min)	97	222	132
Aorta Systolic Pressure (torr)	97	215	106
Aorta Diastolic Pressure (torr)	97	155	65
Aorta Pulse Pressure (torr)	97	61	29
Aorta Mean Pressure (torr)	97	182	83
Mean Venous Pressure (torr)	47	+10	-10
Pulmonary Circulation Time (sec)	57	5.04	3.15
Complete Circulation Time (sec)	57	8.86	5.55
Beats/Complete Circulation	54	24.6	14.3
Blood Volume (ml)	28	827	457
Cardiac Output (liters/min)	49	1.80	0.83
Cardiac Output (liters/kg/min)	49	0.223	0.101
Cardiac Index (liters/m^2/min)	49	3.78	1.75
Systemic Resistance (dyne sec/cm^5)	45	12,870	4,710
Cardiac Work (watts)	45	0.447	0.215
Stroke Volume (ml/beat)	49	10.8	5.9
Stroke Index (ml/beat/kg body wt)	49	1.34	0.67

Table 2

Cardiovascular changes in the pig-tailed monkey #144, Belarius with slow infusion of epinephrine or norepinephrine
Body Weight = 9.8 kg

Time of Day	Aortic Pressures: Systolic torr	Diastolic torr	Pulse torr	Mean torr	Heart Rate beats/min	Aortic Flow Rate in liters/min	Stroke Volume ml	Systemic Resistance (dyne sec/cm^5)	Cardiac Work (watts)
	Pre-infusion control								
1114	120	78	42	103	140	1.75	12.5	4720	.400
1115	Start of epinephrine infusion at a rate of 10 µg/min for 3 minutes								
1118	133	72	61	100	160	2.24	14.0	3580	.498
1130	122	74	48	102	140	1.84	13.1	4490	.416
1131	Start of epinephrine infusion at a rate of 10 µg/min for 1.5 minute								
1133	135	70	65	100	150	2.10	14.0	3830	.468
1148	121	80	41	101	135	1.60	11.9	5060	.359
1149	Start of epinephrine infusion at a rate of 10 µg/min for 2.5 minutes								
1152	138	75	63	102	160	2.35	14.7	3470	.532
1207	123	81	42	100	142	1.80	12.7	4450	.400
	Pre-infusion control								
1341	120	82	46	102	152	1.66	10.9	4910	.375
	Start of norepinephrine (Levophed(R)) infusion at a rate of 5 µg/min for 2.5 minutes								
1347	160	91	69	120	96	1.48	15.4	6500	.395
1403	125	80	45	101	133	1.65	12.4	4900	.370
1403.5	Start of norepinephrine (Levophed(R)) infusion at a rate of 5 µg/min for 1.5 minutes								
1407	158	90	68	118	102	1.47	14.4	6420	.382
1447	120	79	41	100	143	1.70	11.9	4710	.375
1448.0	Start of norepinephrine (Levophed(R)) infusion at a rate of 7 µg/min for 1 minute								
1449.5	168	93	75	125	84	1.42	16.9	7050	.395
1457	122	78	44	100	155	1.72	11.1	4650	.382
Mean values of data									
Control	122	79	44	101	143	1.72	12.1	4740	.385
Epi	135	72	63	101	157	2.23	14.2	3630	.499
Nor	162	91	71	121	94	1.46	15.6	6660	.391

Table 3. Hemodynamic Effects of Hypothermia on Pig-Tailed Monkey #55

Time of Day (hr)	Esophageal Temp. (°C)	Rectal Temp. (°C)	Respiratory Rate (breaths/ min)	Aortic Pressures				Heart Rate (beats/ min)	Cardiac Output (liters/ min)	Stroke Volume (ml)	Systemic Resistance (dyne sec/ cm^5)	Cardiac Work (watts)
				Systolic (torr)	Diastolic (torr)	Pulse (torr)	Mean (torr)					
1126	34.9	35.2	20	157	112	45	136	172	0.67	3.9	16,200	.202
1142	33.7	34.0	17	141	97	44	121	156	0.57	3.7	17,000	.153
1153	31.6	31.9	16	152	106	46	127	132	0.54	4.1	18,800	.139
1208	29.9	29.9	14	155	107	48	132	120	0.46	3.8	23,000	.135
1222	28.2	28.4	14	152	107	45	130	92	0.33	3.6	31,6000	.095
1233	26.8	27.0	16	155	106	49	127	80	0.30	3.8	34,000	.085
1247	25.3	25.6	12	142	100	42	125	76	0.27	3.6	37,100	.075

Table 4. Hemodynamic Effects of Isoproterenol on Pig-tailed Monkey #68, Alexas.

Time of Day	Aortic Pressures				Heart Rate (beats/min)	Cardiac Output (liters/min)	Stroke Volume (ml)	Systemic Resistance (dyne sec/cm^5)	Cardiac Work (watts)
	Systolic (torr)	Diastolic (torr)	Pulse (torr)	Mean (torr)					
	Pre-injection control								
1202	122	79	43	100	176	.767	4.4	10,400	.170
1208	.02 mg Isoproterenol injected								
1210	130	80	50	103	240	.958	4.0	8,600	.219
1223	126	85	41	106	188	.748	4.0	11,400	.176
1338	132	87	45	110	194	.765	3.9	11,500	.187
1341	.032 mg Isoproterenol injected								
1342	118	53	65	86	272	1.028	3.8	6,700	.196
1409	2 ml of 0.9% saline injected								
1410	116	78	38	95	188	.620	3.3	12,500	.131

Table 5. Average Blood Pressures for Two Pig-tailed Monkeys at Berkeley and Barcroft Laboratories

Place	Elevation (feet)	Date	Animal	Time of Day	Aortic Systolic Pressure (torr)	Aortic Diastolic Pressure (torr)	Aortic Mean Pressure (torr)	Left Atrial Pressure (torr)	Pulmonary Arterial Systolic Pressure (torr)	Pulmonary Arterial Diastolic Pressure (torr)
Berkeley	300	1-18 Aug	#49, Claudius	AM	115	78	95	+ 0.3	16	8
				PM	115	77	97	+ 0.7	16	7
			#56, Titinius	AM	112	77	94	- 3.9	17	6
				PM	119	82	99	- 2.9	18	6
Barcroft Laboratory	12,470	19-21 Aug	#49, Claudius	AM	128	88	109	- 0.7	26	11
				PM	126	85	105	- 0.3	26	11
			#56, Titinius	AM	132	91	112	- 0.3	30	13
				PM	127	86	106	+ 0.3	29	12
Barcroft Laboratory	12,470	16-18 Sep	#49, Claudius	AM	98	72	87	- 1.8	22	10
				PM	105	77	92	+ 0.3	27	13
			#56, Titinius	AM	103	73	89	- 0.9	31	16
				PM	110	78	93	- 1.9	38	18
Berkeley	300	19 Sep - 6 Nov	#49, Claudius	AM	102	67	84	+ 2.4	19	8
				PM	89	61	74	+ 3.0	23	9
			#56, Titinius	AM	96	66	80	- 2.2	23	10
				PM	94	63	77	- 3.4	24	9

Table 6. Hemodynamic Summary of the Male Pig-tailed Monkey #293, Chatillon at 750 torr Ambient Pressure

Date	Time	Respiratory Rate (breaths per min)	Heart Rate (beats per min)	Aortic Pressure				Cardiac Output (ml per min)	Stroke Volume (ml)	Systemic Resistance (dyne sec/ cm^5)	Cardiac Work (watts)
				Systolic (torr)	Diastolic (torr)	Pulse (torr)	Mean (torr)				
10 Dec 68	1300	--	--	--	--	--	--	769	--	--	--
	1400	--	--	--	--	--	--	800	--	--	--
	1500	--	--	--	--	--	--	--	--	--	--
	1600	--	--	--	--	--	--	782	--	--	--
	1700	--	--	--	--	--	--	--	--	--	--
	1800	18	184	126	80	46	105	772	4.5	10,256	0.191
	1900	--	180	132	85	47	106	--	--	--	--
	2000	16	180	136	90	46	113	738	4.2	11,910	0.190
	2100	20	192	134	87	47	108	--	--	--	--
	2200	--	188	130	85	45	111	800	4.0	11,858	0.185
	2300	20	198	130	82	48	107	--	--	--	--
	2400	18	184	132	85	47	110	837	4.5	10,365	0.207
11 Dec 68	0100	20	190	131	85	46	110	--	--	--	--
	0200	20	186	133	87	46	107	851	4.6	10,059	0.202
	0300	20	186	137	90	47	113	--	--	--	--
	0400	--	180	142	93	49	115	826	4.6	11,138	0.211
	0500	--	186	138	90	48	110	--	--	--	--
	0600	20	173	142	93	48	115	818	4.7	11,247	0.209
	0700	20	186	125	80	45	100	--	--	--	--
	0800	22	172	130	85	45	113	781	4.5	11,575	0.196
	0900	--	157	133	85	48	112	--	--	--	--
	1000	20	164	140	88	52	115	900	5.5	10,222	0.230
	1100	--	156	135	85	50	114	--	--	--	--
	1200	--	164	133	85	48	113	898	5.5	10,067	0.225
	1300	--	168	137	88	49	117	--	--	--	--
	1400	--	160	136	85	51	115	979	6.1	9,397	0.250
	1500	18	161	--	--	--	--	--	--	--	--
	1600	18	172	135	85	50	115	933	5.4	9,861	0.238
Mean		19	177	134	86	48	111	832	4.8	10,663	0.211

Table 7. Hemodynamic Record of #293, Chatillon during Ascent to Simulated Altitude, 11 December 1968

Ambient Pressure	Sea Level (750 Torr)	654 Torr	600 Torr	550 Torr	500 Torr	460 Torr
Respiratory Rate (breaths/min)	18	24	24	24	25	32
Heart Rate (beats/min)	172	176	174	178	176	182
Aortic Systolic Pressure (torr)	135	136	142	142	142	132
Aortic Diastolic Pressure (torr)	85	88	90	90	90	82
Aortic Pulse Pressure (torr)	50	48	52	52	52	50
Aortic Mean Pressure (torr)	115	114	117	117	118	107

Table 8. Hemodynamic Summary of the Male Pig-tailed Monkey #293, Chatillon at 460 torr Ambient Pressure

Date	Time	Respiratory Rate (breaths per min)	Heart Rate (beats per min)	Aortic Pressure				Cardiac Output (ml per min)	Stroke Volume (ml)	Systemic Resistance (dyne sec/ cm^5)	Cardiac Work (watts)
				Systolic (torr)	Diastolic (torr)	Pulse (torr)	Mean (torr)				
11 Dec 68	1700	--	180	127	75	52	102	--	--	--	--
	1800	--	175	124	77	47	101	957	5.5	8,443	0.215
	1900	--	176	113	66	47	95	--	--	--	--
	2000	--	180	116	74	42	98	937	5.2	8,367	0.204
	2100	--	180	117	74	43	98	--	--	--	--
	2200	--	180	113	72	41	95	1,144	6.4	6,643	0.241
	2300	--	172	122	77	45	101	--	--	--	--
	2400	--	168	123	77	46	100	943	5.6	8,484	0.209
12 Dec 68	0100	--	166	121	77	44	98	--	--	--	--
	0200	--	162	121	75	46	97	901	5.6	8,613	0.194
	0300	--	174	120	77	43	103	--	--	--	--
	0400	--	168	118	75	43	100	921	5.5	8,686	0.204
	0500	--	162	121	77	44	105	--	--	--	--
	0600	--	164	121	77	44	103	871	5.3	9,460	0.199
	0700	--	156	118	74	44	98	--	--	--	--
	0800	--	164	112	68	44	88	846	5.2	8,322	0.165
	0900	--	156	120	77	43	102	--	--	--	--
	1000	--	164	117	73	44	98	--	--	--	--
	1100	--	164	112	67	45	85	--	--	--	--
	1200	--	160	112	70	42	90	1,026	6.4	7,016	0.205
	1300	--	156	116	75	41	95	--	--	--	--
	1400	27	156	120	75	45	98	972	6.2	8,066	0.211
	1500	30	164	122	80	42	103	--	--	--	--
	1600	30	160	120	76	44	100	868	5.4	9,217	0.193
Mean		29	167	118	74	44	98	944	5.6	8,301	0.204

Table 9. Hemodynamic Record of #293, Chatillon during Descent from a Simulated Altitude, 12 December 1968

Ambient Pressure	460 Torr	500 Torr	550 Torr	600 Torr	650 Torr	700 Torr	Sea Level (750 Torr)
Respiratory Rate (breaths/min)	36	27	23	24	27	27	30
Heart Rate (beats/min)	162	160	178	175	174	175	168
Aortic Systolic Pressure (torr)	125	130	130	130	125	122	127
Aortic Diastolic Pressure (torr)	77	82	80	80	75	70	80
Aortic Pulse Pressure (torr)	47	47	50	50	50	52	47

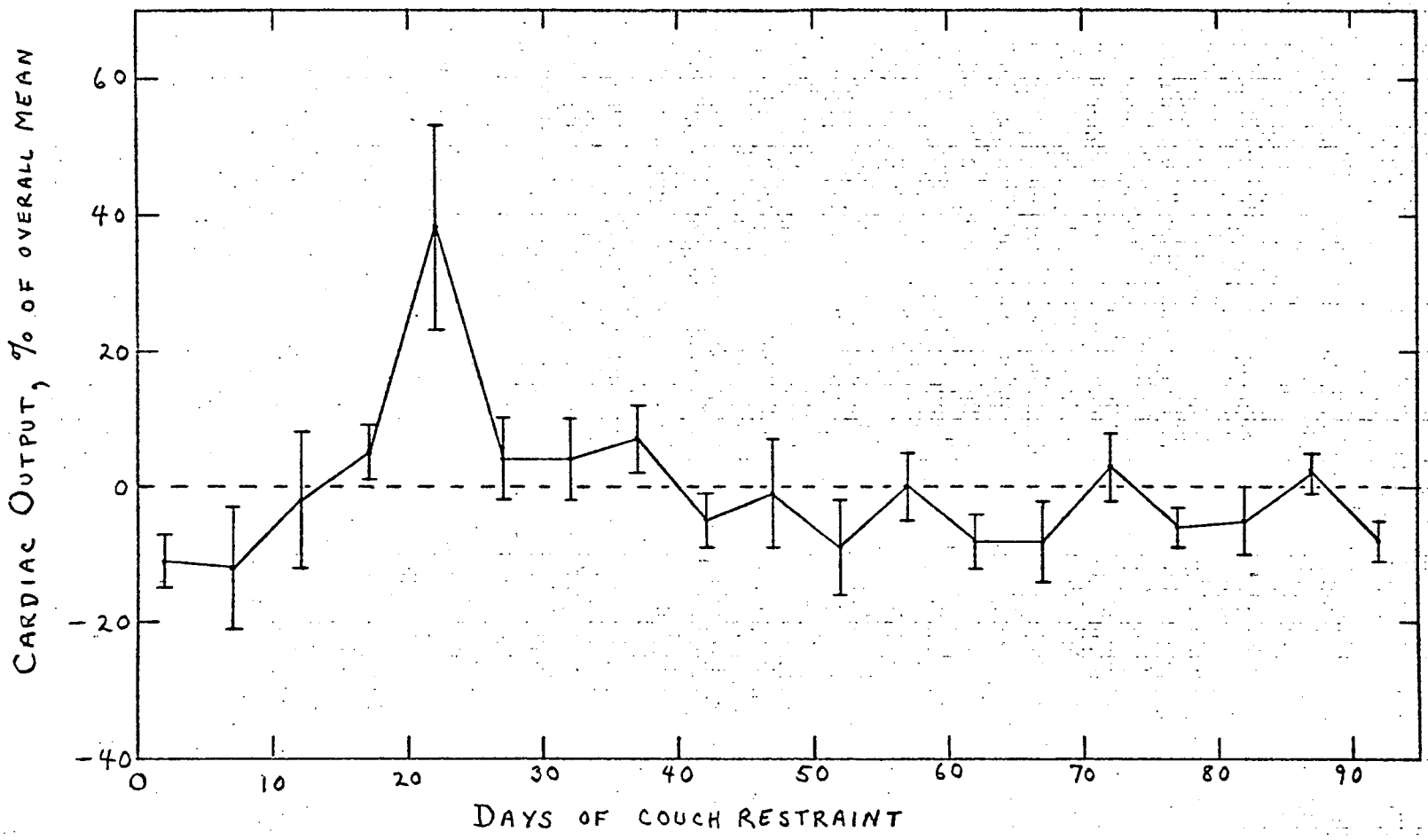


FIG. 1. MEAN CARDIAC OUTPUT OF 4 PIG-TAILED MONKEYS DURING CONTINUOUS COUCH RESTRAINT, EXPRESSED AS PER CENT OF MEAN OF ALL VALUES. BARS INDICATE ± 1 S.E.

Table 10. Effect of Blood Removal and Return on Heart Rate and Blood Pressure in Pig-tailed Monkey #62. Body Weight 9.0 kg.

Day of Continuous Restraint	Time of Day	Volume or Blood Withdrawn (ml)	Before Removal		During Removal	End of Removal		During Return	End of Return	
			Heart Rate (beats/min)	Aortic Pressure syst/diast (torr)	Heart Rate (beats/min)	Heart Rate (beats/min)	Aortic Pressure syst/diast (torr)	Heart Rate (beats/min)	Heart Rate (beats/min)	Aortic Pressure syst/diast (torr)
44th	1417	16.5	160	135/82	160	--	--	160	160	143/85
	1429	16.5	160	137/77	154	--	--	154	160	125/73
	1447	16.5	164	150/86	160	--	--	160	160	138/81
65th	1431	17	188	157/91	184	188	148/91	192	192	166/95
	1447	14.5	184	156/90	184	--	--	184	186	161/86
	1505	13.5	188	161/97	182	180	154/91	184	180	157/90
67th	1433	30	164	134/76	168	176	141/83	168	164	140/79
	1447	15	168	137/79	172	172	136/80	188	184	148/84
	1506	20	182	147/90	180	188	148/89	192	184	147/83
	1525	30	184	136/84	192	190	142/86	192	192	150/85
72nd	1450	17	188	125/79	192	--	--	192	188	144/79
	1505	30	190	136/78	192	192	133/77	192	192	132/74
	1522	30	184	130/75	188	188	138/82	190	188	134/75
74th	1538	30	176	131/74	172	172	122/72	172	172	131/71
	1556	30	172	137/78	172	172	129/75	172	176	126/70
79th	1553	30	192	142/81	192	200	150/91	196	196	132/81
	1610	30	192	141/95	192	196	151/87	196	194	142/83
	1624	30	202	154/88	198	198	146/89	196	208	163/89
81st	1500	30	180	132/76	188	184	130/79	192	180	135/77
	1516	30	188	144/82	184	--	--	--	--	--
	1535	30	192	150/89	188	188	137/84	188	192	155/85
88th	1502	30	172	147/83	172	172	137/81	188	176	147/81
93rd	1415	30	170	147/87	170	172	147/88	172	172	152/86

Table 11. Comparison of blood flow rate in the ascending aorta as recorded by an electromagnet flow meter and cardiac output determined by dye dilution (#136, Angelo)

Observation No.	Method of Cardiac Output Determination		Difference Dye Dilution minus Flow Probe	
	Dye Dilution (ml/min)	Flow Probe (ml/min)	ml/min	% diff.
1	960	900	+ 60	6.25
2	730	750	- 20	2.74
3	950	925	+ 25	2.63
4	980	1090	-110	11.22
5	1150	1040	+110	9.57
6	1110	1060	+ 50	4.51
7	1020	1000	+ 20	1.97
8	1120	1080	+ 40	3.54
9	900	925	- 25	2.78
10	1070	925	+145	13.55
11	1260	1100	+160	12.70
12	1090	1040	+ 50	4.58
13	1000	1050	- 50	5.00
14	1135	1070	+ 65	5.73
15	1000	1150	-150	15.00
16	910	900	+ 8	0.88
17	905	1020	-117	12.92

Range of % differences: 0.88% - 15.00%

Number of comparisons with less than 10% difference = 12 or 71%.

Table 12. Comparison of the blood flow rate in the ascending aorta as recorded by an electromagnetic flow meter and cardiac output determined by dye dilution (#144, Belarius).

Observation No.	Method of Cardiac Output Determination		Difference Dye Dilution minus Flow Probe	
	Dye Dilution (ml/min)	Flow Probe (ml/min)	ml/min	% diff.
1	1165	805	+ 306	26.26
2	1295	880	+ 415	32.05
3	955	720	+ 235	24.61
4	1225	1250	- 25	2.04
5	1230	1240	- 10	0.81
6	1485	1290	+ 195	13.13
7	1615	1710	- 85	5.26
8	1305	1640	- 335	25.67
9	1520	1650	- 130	8.55
10	1325	1670	- 335	25.28
11	1235	1640	- 405	32.79
12	1145	1685	- 540	47.16
13	1330	1820	- 490	36.84
14	1920	2170	- 250	13.02
15	1650	2100	- 450	27.27
16	1485	1750	- 265	17.84
17	1075	1510	- 435	40.46
18	1275	1650	- 375	29.41
19	1880	1900	- 20	1.06
20	1570	1970	- 400	25.48
21	1480	1900	- 420	28.38
22	1600	1645	- 45	2.81
23	1060	1560	- 500	47.17
24	2300	1960	+ 340	14.78
25	1825	2110	- 285	15.62
26	1780	2090	- 310	17.42

Range of % difference from dye dilution method = 0.81% - 47.17%

Number of comparisons with less than 10% difference = 6 or 23.08%

Table 13. Comparison of Cardiac Output as Determined by the PHAMOS Catheter Cuvette and the Gilford Densitometer

Monkey	Date	Cardiac Output in ml/min		Per Cent Difference of PHAMOS from Gilford
		PHAMOS	Gilford	
#18, Escalus	3 Jan 67	1400	1509	- 7.2
		1347	1203	+ 12.0
		1682	1682	0.0
		1831	1745	+ 8.2
		1555	1610	- 3.6
		1473	1394	+ 5.7
		1586	1531	+ 3.6
		1581	1739	- 12.4
		1524	1630	- 7.1
		1616	1696	- 4.7
#160, Surrey	6 Jan 67	917	787	+ 16.5
		977	901	+ 8.4
		1190	1099	+ 8.3
		1003	958	+ 4.7
		1145	1149	- 0.3
#145, Leonatus	11 Jan 67	1216	1236	- 1.6
		1154	1181	- 2.3
		1253	1354	- 7.5
		1129	1143	- 1.2
		1111	1128	- 1.5
n = 20	Mean	1325	1334	

Table 14

Measurement of Total Blood Volume as Determined by Extrapolation to Zero Time from the Recycling Dye Dilution Curve

Animal No.	Body Weight (kg)	Blood Volume	
		Total (ml)	ml/kg body wt.
32	7.82	510	65.2
	7.82	538	68.8
	7.82	487	62.3
27	9.40	653	69.5
	9.40	621	66.1
	9.40	615	65.4
	9.40	645	68.6
	9.40	615	65.4
	9.40	630	67.0
	9.40	659	70.1
48	8.13	659	81.0
24	6.90	425	61.5
	6.90	428	62.0
	6.90	440	63.8
	6.90	431	62.5
	6.90	443	64.2
	6.90	433	62.7

Table 15. Simultaneous Determinations of Red Cell Mass and Plasma Volume in Six Pig-tailed Monkeys.

Monkey	Body Weight (kg)	Red Cell Volume (ml/kg body wt)	Plasma Volume (ml/kg body wt)	Whole Blood Volume (ml/kg body wt)	Aortic Hematocrit Value (%)	Computed Whole Body Hematocrit Value (%)	Ratio of Whole Body Hematocrit to Aortic Hematocrit (F_{cells})
#145, Leonatus	6.35	19.6	34.0	53.6	38	36	0.96
#171, Snare	7.50	16.9	42.0	58.9	41	29	0.69
#175, Salisbury	5.52	18.2	46.1	64.2	33	28	0.85
	5.10	13.5	51.4	64.9	28	21	0.75
#178, Fluellen	7.30	19.3	63.9	83.2	35	23	0.66
#179, Jamy	5.10	18.4	46.7	65.0	33	28	0.85
#181, Court	7.05	19.7	36.5	56.2	41	35	0.86
Mean	6.27	17.9	45.8	63.7	36	29	0.80

Table 16. Plasma Proteins in 10 Pig-tailed Monkeys

Monkey No.	Total Protein (g/100 ml)	Albumin (g/100 ml)	α_1-Globulin (g/100 ml)	α_2-Globulin (g/100 ml)	β_1-Globulin (g/100 ml)	β_2-Globulin (g/100 ml)	γ-Globulin (g/100 ml)	Fibrinogen (g/100 ml)
171	6.60	2.41	0.74	0.44	0.56	0.30	1.20	0.94
188	7.36	1.93	0.94	0.54	0.77	0.34	1.30	1.55
210	7.95	2.48	0.78	0.42	0.78	0.29	1.76	1.42
222	7.42	2.29	0.62	0.20	0.79	0.99	1.45	1.08
223	6.50	2.00	0.70	0.75	0.62	0.22	1.23	0.97
230	8.20	2.71	0.85	0.73	0.62	0.54	1.32	1.40
232	7.71	2.67	1.03	0.49	0.67	0.58	0.80	1.46
2	6.55	1.92	0.66	0.99	(0.62)		1.22	1.15
175	7.10	2.17	0.70	1.01	(0.76)		1.38	1.08
198	8.20	2.35	0.93	0.66	(1.21)		1.28	1.79
$\bar{X}$	7.36	2.29	0.80	0.62	0.69 (0.86)	0.47	1.29	1.28

Table 17. Ventilatory and related blood chemical base-line data from pig-tailed monkey #144, Belarius breathing room air during continuous restraint.

Date	Minute Volume liters/min		Tidal Volume liters		Respiratory Rate breaths/min		Arterial P_{O_2} torr		Arterial pH	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range
7 Jun 66					28 (3)*	24-32	90 (5)	88-92		
8 Jun 66					32 (4)	28-44	94 (4)	91-96		
9 Jun 66					35 (3)	32-36	92 (3)	91-94		
10 Jun 66					39 (8)	34-44	89 (12)	81-94		
15 Jun 66					39 (4)	36-48	92 (4)	88-97	7.49	7.48-7.51
16 Jun 66					26 (4)	24-28	95 (7)	93-97	7.48 (3)	
20 Jun 66					33 (6)	28-38	93 (15)	89-97	7.50 (18)	7.45-7.53
22 Jun 66							94 (3)	91-96	7.47 (4)	7.45-7.49
23 Jun 66	2.97 (6)	2.64-3.33	.069	.060-.075	43	41-44	93 (3)	91-94	7.48 (3)	7.47-7.49
24 Jun 66	3.18 (3)	2.96-3.58	.068	.060-.080	47	37-55	86 (1)		7.40 (1)	
29 Jun 66	3.35 (4)	3.23-3.52	.091	.085-.095	37	36-38				
6 Jul 66	3.80 (3)	3.60-4.10	.080	.075-.085	48	47-49			7.56 (4)	7.54-7.57
7 Jul 66	2.86 (2)	2.80-2.92	.067	.064-.071	43	41-46				
11 Jul 66	3.25 (5)	2.88-3.57	.083	.072-.105	39	34-43				
17 Jul 66	2.85 (5)	2.55-3.00	.083	.078-.088	34	32-37				
25 Jul 66	2.83 (3)	2.66-3.12	.068	.067-.076	42	41-43	86 (2)			7.46

* Figures in parentheses refer to the number of observations made.

Table 17A. Ventilatory and related blood chemical base-line data from pig-tailed monkey #141, Cominius breathing room air during continuous restraint.

Date	Minute Volume liters/min		Tidal Volume liters		Respiratory Rate breaths/min		Arterial P_{O_2} torr		Arterial pH	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range
19 Jul 66	2.61 (4)*	2.52-2.69	.075	.068-.082	36	33-38	86 (2)		7.53 (2)	
20 Jul 66	2.95 (3)	2.80-3.14	.091	.082-.097	33	33-34				
21 Jul 66	3.34 (3)	3.15-3.60	.084	.073-.090	40	37-43	87 (7)	85-89	7.52	7.47-7.58
22 Jul 66	2.58 (3)	2.29-2.75	.070	.068-.072	37	34-39	89 (3)	81-94	7.52	7.51-7.54
27 Jul 66	3.75 (5)	3.50-3.90	.100	.095-.106	37	36-39				

* Figures in parentheses refer to number of observations.

Table 18. Blood gas analysis of six adult male pig-tailed monkeys*

Monkey	Aorta			Pulmonary Artery		
	pO_2 torr	pCO_2 torr	pH	pO_2 torr	pCO_2 torr	pH
#2, Bottom	115.0	34.8	7.478	42.5	43.3	7.425
#145, Leonatus	108.5	41.5	7.475	30.0	49.3	7.418
#171, Snare	105.5	37.8	7.490	43.5	43.8	7.440
#175, Salisbury	102.5	35.3	7.503	32.0	38.8	7.455
#178, Fluellen	109.3	35.0	7.487	33.0	46.8	7.415
#181, Court	104.8	38.0	7.480	38.5	45.3	7.435
Mean Value	107.6	37.1	7.486	36.6	44.6	7.431

Table 19. Oxygen hemoglobin dissociation curve data for six male pig-tailed monkeys.

Monkey	pO_2 torr level						
	14	24	31	42	56	71	85
	Per cent saturation of hemoglobin at various levels of oxygen partial pressure						
#2, Bottom	22.6	35.1	46.6	66.4	81.9	92.7	97.6
#171, Snare	17.9	29.0	43.5	55.5	77.7	88.6	97.5
#178, Fluellen	19.5	31.5	40.4	59.3	77.7	86.8	97.8
#181, Court	23.6	37.5	47.5	68.0	86.2	97.2	100.0
#184, Charles	15.2	30.1	45.0	62.6	77.8	91.2	93.7
#187, Orleans	19.8	33.3	47.4	67.3	82.7	96.7	100.0
Mean	19.8	32.8	45.2	63.2	83.7	92.2	97.8
Standard Deviation	2.8	2.3	1.8	3.8	2.2	3.8	1.1
Standard Error	1.14	0.94	0.74	1.55	0.90	1.55	0.45

Table 20. Changes in Aortic Partial Pressure of Oxygen with Varying Ambient Air Pressures Recorded from a Chronically Implanted Sensor in the Male Pig-tailed Monkey #275, Cornwall

Ambient Air Pressure (torr)	Oxygen Partial Pressures			Saturated Air pO_2 minus Aortic Blood pO_2 (torr)
	Dry Air (torr)	Saturated Air (torr)	Aortic Blood (torr)	
754	157	147	92	55
700	146	135	82	53
650	135	125	76	49
600	125	115	67	48
550	114	104	52	52
500	104	94	44	50
450	94	84	38	46
425	87	78	35	43
450	94	84	37	47
500	104	94	39	55
550	114	104	50	54
600	125	115	58	57
650	135	125	70	55
700	146	135	85	50
754	157	147	102	45

Table 21. Dynamic Ranges for Heart Rate and Mean Aortic and Pulmonary Artery Blood Pressures Before and During Centrifugation (up to 12 *g*)[1]

	Heart Rate beats/min	Blood Pressure (torr)	
		Aortic	Pulmonary Artery
Before (rest)	165-230	82-130	9-16
Centrifugation (up to 12 *g*)	195-250	130-259	9-102

[1] Data compiled from six animals.

ENGINEERING CONSIDERATIONS

1. Introduction.

This report presents an engineering discussion of the Phase II Task A study of the Automated Hemodynamic Subsystem (AHS) as it exists currently. Additions and deletions will be made as progress of the engineering-biology interface demands.

Study Approach - Technical requirements will be derived from the scientific guidelines furnished by the biologists. These data will be used for analyses and design to develop a configuration base line for the AHS concepts. Alternate approaches and concepts will be studied to avoid uncertain state-of-the-art development or techniques. Trade studies will be performed in collaboration with the scientific staff to ensure that the optimum base line concept is chosen for the AHS. Commercially available flight qualified hardware that is already proven to be reliable will be used whenever possible.

Responsibility - The chief engineer will have responsibility for integrity of engineering design.

Program Approach - The engineering approach to the AHS development will be to safeguard the scientific data validity of the system, and to meet fully and effectively its technical requirements embodied in a fail safe design. The development of engineering hardware is not the purpose of this program. It is the biological experiment that is most important and therefore its needs must determine the guidelines.

2. Scientific and Technical Integration Plan.

To attain the primary objectives of the Automated Hemodynamic Subsystem, a proposed operational plan has been developed. This defines by task the specific areas and where a mutually effective team participation is required. A further expansion of the effort is included in Task Descriptions, grouped as follows:

Task Descriptions

Reliability, Analyses and Criteria

System Engineering and Integration

Review and Summary

2.1 System Engineering and Integration - System engineering and integration shall be conducted through close collaboration and coordination between all members of the APRL team. To ensure systematic development of the Automated Hemodynamic Subsystem, the engineering process shall be based on the data indicated in this document.

2.2 Reliability Analyses and Criteria - The reliability concepts will be blended with the conceptual studies through the close association of reliability and design concepts. As Phase IIA progresses, a reliability value will evolve based upon trade studies and system development.

The design review activity will be continuous to assure a high reliability and confidence level in the final design. It also provides an opportunity to coordinate ideas between the engineering elements of the working team, and provides the means for carrying out reliability disciplines into each design phase.

2.3 Task Descriptions - Engineering will provide the support and services necessary to accomplish the following effort.

2.3.1 Liaison - Engineering will maintain a close technical liaison with the science coordinator to assure an optimization of the proposed items of work.

2.3.2 APRL Systems - To facilitate the analyses of the design concepts, it is necessary to consider all interfacing subsystems. Appropriate techniques will be used to ensure the orderly development of base line criteria and to study the interaction between the AHS and other subsystems. Those subsystems having the closest interface are the Bio-Module, Experiment Envelope, and Environmental Control Subsystem.

2.3.3 Technical Documentation and Reports - Documentation for this study effort will be provided to define an AHS configuration base line design concept and performance criteria. Analysis summaries and configuration study drawings will be provided, as appropriate, to substantiate and further define the concepts selected. Specific items for submittal will be:

AHS design and criteria specifications.

Definition of AHS configuration base line design concept, with summarized analyses and configuration study drawings.

2.3.4 Master Schedule

2.4 Review and Summary - The results of Phase IIA will be the consequence of considerable effort, and will be necessary for Phase IIB development and progress. As such, they are essential products generated by certain activities or functions under certain boundary conditions and constraints.

2.4.1 Boundary Conditions and Constraints - The boundary conditions and the constraints that serve to direct the AHS base line include:

Requirement for scientific validity of acquired data.

Requirement for the scientific integrity of the complete subsystem.

Requirement for the AHS to operate automatically and continuously for 60 days, but with the capability for 90 days in the unattended mode. Requirement for the AHS to be ultimately suitable for a 60-day space mission.

Requirement of "mean time between failures" and "burn in" time.

2.4.2 Functions - The various functions which will be performed to define the preliminary base line of the AHS will be analytical, evaluative, and studied, in nature. These functions, which may have more than one output as a product, include:

The acquisition of information and data pertinent to design.

Assessment of the present state of the art hardware.

Trade study effort to determine an optimal design concept.

Evaluation of component suitability in terms of performance characteristics.

Evaluation of component suitability in terms of experiment procedure compatibility.

Evaluation of component-to-component compatibility in terms of APRL requirements.

2.4.3 Products - The products include:

Presentation of AHS design concepts.

Definition of general engineering criteria essential for design of the AHS.

Evaluation of the compatibility between the monkey/subsystem interface.

Evaluation of the compatibility between component-to-component interface, for component-to-subsystem interface, and for subsystem-to-APRL interface.

Circumscription of the major problem areas.

Identification of the high risk areas.

Definition of subsystem preliminary base line design.

3. Physiology/Engineering Interface.

The APRL is an orbital laboratory for the study of environmental physiology. The research objective is the investigation of physiological effects of weightlessness.

3.1 Hemodynamic Function - The term hemodynamic function is intended to cover the various aspects of cardiovascular and respiratory activity that will be measured. These include not only the physiological characteristics of the pumping action of the heart and flow of blood through the main vessels of the circulation, but also include the estimation of the degree of oxygenation of the blood, of the concentration of blood hemoglobin and total plasma protein, and of the temperature of the blood as it leaves the heart.

During the continuous period of days in the weightless state, the normal hydrostatic loading of the blood circulatory system will be absent. It therefore becomes important to establish the extent of the changes qualitatively expected to occur in hemodynamic function.

3.1.1 Cardiac Output - The outflow rate, termed the cardiac output, is found to vary from 0 to 3.00 liters/min, depending upon the physiologic state of the monkey. At any particular time, the cardiac output value is determined by a number of complex, interacting reflex processes.

During Phase I of the several methods available for the continuous measurement of cardiac output led to the selection of the dye-dilution principle as the most accurate and reliable technique available. In this method, a precisely known quantity of a green dye, indocyanine green, is injected intravenously, and the time course of change in blood concentration

of the dye in an artery is determined for a period of some seconds after injection. From the average arterial concentration of the dye, the cardiac output may readily be calculated. Indocyanine green exhibits a light absorption maximum at 805 mμ, which is also the wavelength of the isobestic point of the blood hemoglobin.

A procedure has been developed for the chronic implantation of catheters in the vena cava and aorta which makes possible the repeated intravenous injection of indocyanine green and withdrawal of arterial blood for dye concentration measurement.

The arterial blood dye concentration is measured directly in the arterial catheter by means of a silicon photodiode transducer which senses changes in optical density at 805 mμ, the absorption maximum for indocyanine green. An identical photo-transducer is applied to the venous catheter to monitor the injected dye concentration.

The goal for the Phase II design effort is to make duplicate cardiac output determinations five minutes apart every 6 hours for 60 days of test. The automated cardiac output apparatus will contain sufficient dye for this purpose. From such data it will be possible to define any changes which may occur in the general level of the resting cardiac output.

In order to test hemodynamic responsivity to a load imposed on the cardiovascular system, it is also proposed to measure cardiac output in the subject animal during the application of reduced ambient air pressure to the lower half of the body for a brief period at intervals of 4 days throughout the 60-day test. The maneuver may be accomplished by a reduction in ambient air pressure of about 40 torr applied for 40 seconds. The cardiac output would be measured during the last 20 seconds of the reduced pressure period.

3.1.2 Blood Pressure - By measuring the mean blood pressure in the aorta and vena cava, together with the cardiac output, it is possible to apply a simple equation and compute the total peripheral resistance of the systemic circulation, as follows:

$$R = \frac{P_A - P_V}{Q}$$

where R is the total peripheral resistance, P_A the mean aortic pressure, P_V the mean vena cava pressure, and Q the cardiac output.

In addition to the two catheters in the aorta and vena cava, there will be chronic catheters in the pulmonary artery and left atrium of the subject animal so that blood pressures in the pulmonary circulation may also be monitored. Thus, the subject animal will be equipped with four vascular catheters. Statham strain-gauge pressure transducers through the link of the fluid-filled catheters are used to sense the pressure fluctuations in the vascular system at this time, however numerous other transducers lend themselves to the application.

3.1.3 Heart Rate and Electrocardiogram - Heart rate can be conveniently determined from the continuous monitoring of the blood pressure wave forms. A direct implant with T/M (or hard wire) can be used as well as the external methods now in lab use. It is also obtained from a recording of the body electric potential changes which accompany the muscular contraction events in the heart, termed the electrocardiogram or EKG.

3.1.4 Total Plasma Volume - In the pig-tailed monkey, the intravascular mixing time of dye has been found to be completed within 60 seconds after injection.

In the case of indocyanine green, the dye is simultaneously being cleared from the circulation by the liver as it mixes, and the clearance

halftime in the monkey is approximately 100 seconds. If measurement of the arterial concentration of indocyanine green is continued after the intravascular mixing process is completed, i.e., from 60 to 120 seconds after dye injection, it is possible to establish the plasma dye clearance curve. This curve may be extrapolated back to zero time, and the intercept concentration value may be used to compute total blood volume with acceptable accuracy.

The complete indocyanine green dye cycle with base line reference is four minutes, two minutes of which is the arterial blood withdrawal phase and two minutes the blood reinjection phase. The continuous measurement of dye concentration during the withdrawal phase by light absorption at 805 mμ permits determination of both cardiac output and total blood volume.

3.1.5 Blood Hemoglobin Concentration - The arterial blood withdrawal phase is started 20 seconds before dye injection is made to provide a base line for the cardiac output determination. Because the light absorption measurement is made at 805 mμ at the isobestic point of the oxyhemoglobin and reduced hemoglobin absorption spectra, the optical density of the preinjection base line can be interpreted to yield blood hemoglobin concentration. This permits evaluation of hemoglobin level every 6 hours.

3.1.6 Systemic Arterial Oxygen Saturation - The light absorption spectra for oxyhemoglobin and reduced hemoglobin are quite different but cross at 805 mμ, the isobestic point. By measuring optical density at this wavelength, the total concentration of hemoglobin may be determined, irrespective of its degree of oxygenation. On the other hand, at 660 mμ reduced hemoglobin is strongly absorbent, whereas oxyhemoglobin is quite transparent. Therefore, by measuring the optical density of blood at 660 mμ as well as 805 mμ, it is possible to determine the percentage of the total

hemoglobin which is oxygenated.

A silicon photodiode transducer which measures optical density at 660 mμ will be applied to the aortic catheter, and its output will be combined electronically with that from the 805 mμ transducer to yield systemic arterial oxygen saturation.

3.1.7 Pulmonary Arterial Oxygen Saturation - The pulmonary artery contains the mixed venous blood from the systemic circulation, and measurement of its degree of saturation with oxygen, together with systemic arterial blood oxygen saturation measurement, permits the computation of the arterio-venous oxygen difference. This value is used in assessing oxygen delivery by the blood to the body tissues.

Two silicon photodiode transducers will be applied to the pulmonary artery catheter to measure the mixed venous blood (optical density at 660 mμ and 805 mμ). This will permit evaluation of the per cent saturation with oxygen of the mixed venous blood. From this value and the systemic arterial blood oxygen saturation, it will be possible to compute arterio-venous oxygen difference in cm^3 oxygen per 100 ml of blood.

3.1.8 Total Plasma Protein Concentration - Functional operation date not predictable at this time.

3.1.9 Aortic Blood Temperature - It is recognized that the various tissues and organs of the body have widely different rates of heat production on an equal weight basis, and evidence of this may be found in the different temperatures which may be recorded locally in the various parts of the body.

Continuous measurement of aortic blood temperature will be considered by engineering for the body heat regulatory mechanism, and for defining "body temperature".

In Phase I, it was found to be feasible to incorporate a thermistor into the tip of the aortic catheter, from which satisfactory continuous temperature recordings were made. It is planned to consider this feature for the Phase II test animals. As an alternate procedure, surgical implantation of a battery-operated, completely sealed temperature telemetry capsule is also contemplated and being tested in the Bonita Laboratory at present.

3.1.10 Temperature of Blood Vessel Walls - Initially, it was proposed to measure the temperature of the blood directly in vascular bed. By using two thermocouples, one within the bloodstream and the other placed appositionally but on the outer blood vessel wall, a small difference of 0.1°C was noticed. However, this was deemed insignificant when compared to the added problems of maintaining a sensor within a blood vessel.

3.1.11 Automated Hemodynamic Unit - The various hemodynamic measurements frequently involve complex techniques, and those suitable for the APRL can be performed only with direct surgical access to the cardiovascular system. Thus, indwelling vascular catheters will be placed in the: (1) thoracic aorta, (2) anterior vena cava, (3) pulmonary artery, and (4) left atrium. The engineering hardware will interface with these catheters.

4. Subsystem Design Concept.

The Automated Hemodynamic Subsystem will be designed to comply with the requirements as specified by the scientific staff and the Principal Investigator, based on the initial design work accomplished by the conceptual design book for APRL but will not be restricted to the limited design concepts.

The function of this subsystem is to obtain scientific hemodynamic data with minimal physiological effect on the monkey.

In order to maintain integrity and data validity, not only the biological factors involved in the blood pressure measurement, dye injection, heparinized saline solution injection, and blood withdrawal/injection must be considered, but also the material compatibility, temperature control, and sterilization.

Blood pressure measurements are to be made on each of the four catheters entering the Bio-Module. These are isolated from the blood by a plastic interface material which is capable of transmitting minute pressure changes via a "bubble expansion" to captive fluid directly coupled to a pressure transducer or a pressure implant in the connector. Transmitting pressure changes by this method minimizes the possibility of blood hemolysis and/or coagulation.

The dye injection mechanism, which is used to determine total plasma volume and cardiac output, consists of a solenoid actuated spring-filled dye injector, a valve, and a dye reservoir. The valve permits intermittent dye injector filling, dye injection into the vena cava catheter, and heparinized saline flushing of the dye into the right atrium. The injector is a positive displacement calibrated syringe which will deliver precise quantities. The injection rate into the catheter is controlled by a sized orifice outlet. The dye is forced through the catheter into the vena cava at a controlled rate by a positive displacement pump. A densitometer is used to determine the concentration of the injected dye.

Heparinized saline solution is utilized for flushing all blood residue from the syringe and for clearing of catheter terminations as well as dye injection.

Twice (5 minutes apart) during each six-hour period, blood is withdrawn and reinjected into the aorta to determine cardiac output and associated measurements and the pulmonary artery for oxyhemoglobin concentration. The pump uses a ball-nut screw-driven piston to discharge heparinized saline solution for flushing the blood syringe and catheter. The piston is sequenced to stop just prior to bottoming out on the end of its cylinder to allow for satisfactory flushing and prevent hemolysis of red blood cells.

Blood cell damage may be caused by sharp edges, tool marks, and/or rough surface areas that are in contact with the blood. Care must be taken to ensure smooth interfaces and elimination of turbulence at the catheter-component connections as well as limit the number of these connections. One of the types of connectors which has been investigated is the Clay-Adams heat flared connector (which is a Luer-Slip adapter for plastic tubing). The male portion of this connector is machined on the syringe and/or valve body of a blood-compatible material. The catheter is passed through the metal female half of the connector and is heat flared by holding it close to, but not in, an open flame. This connector appears to offer minimal interface disturbances.

Incompatibility of materials can damage the blood of the monkey and possibly cause a premature experiment termination. All components which are contacted by dye, blood, and/or heparinized saline must be made of accepted body fluid compatible materials. The criteria for the evaluation of material selection must be established from the physical requirements of the blood and the acceptable sterilization methods. Materials selected must be tolerant of the temperatures and chemicals that may be used to maintain sterile conditions, and must not be conducive to blood clotting

and/or contamination. The material/blood compatibility data is basic to the design trade studies.

Due to the frequent blood withdrawal/injection cycles, it will be necessary to control the temperature of the blood withdrawal unit to be compatible with the monkey's temperature (38°C) to prevent excessive body heat transfer. This temperature control must also be applied to the dye injection unit and any heparinized saline which is injected in the monkey's blood vessels. It is assumed the Experiment Module and Bio-Module temperatures will be below the 38° temperature of the monkey; therefore, heat will always be added to the blood withdrawal and injection unit.

HEMODYNAMIC SUBSYSTEM

1) The Hemodynamic Subsystem is unique in its requirements in that the blood withdrawn from the monkey must be returned to the animal in "acceptable" condition.

2) A blood withdrawal rate of 5 to 18 ml/min for 60 sec after dye injection.

3) A blood withdrawal rate of 5 to 18 ml/min for 60 sec before dye injection.

4) A total of 30 ml maximum in withdrawal syringe to allow for the 130 seconds should be the design goal.

5) The valving would be best if it is designed for "fail safe" operation in the event that the "withdrawal mode" or "return mode" is either partially or fully completed when "operational" failure occurred.

6) The heparinized saline solution should not leak into the blood catheter at a rate of more than 1 drop/24 hrs.

7) Full flow into the blood catheter from the flushing syringe would be best if arranged to function only on "command" from the inboard programmer.

8) The Hemodynamic Subsystem temperature design goal should be 38° $\pm$ 0.5°C to avoid thermal shock to the monkey.

9) The functional capability of the Hemodynamic Subsystem must have the capacity of 15 days pre-orbital, 60 days orbital, and 15 days post-orbital.

10) The materials in this subsystem must be non-wetting, corrosion free, compatible with fluids contacted, have producibility, and be mechanically and chemically stable; e.g., PPO, Kel-F, Teflon, Polycarbonate, and type 316 St Steel.

11) The blood's pressure may reach 300 torr for the aorta.
" " " " " -10 to +10 torr for the vena cava.
" " " " " -0 to +100 torr for the pulmonary artery.
" " " " " -10 to +10 torr for the left atrium.

12) The predetermined physical characteristics of the syringe are:
capacity 40 ml
piston diameter 25 mm for the travel speed now used; however, a larger piston can be considered and moved at a slower rate.
inlet to syringe 0.85 mm ID (1.25 mm ID is now working successfully).
the piston surge shall not exceed collapse pressure on withdrawal of -60 torr; on return of +60 torr (based on std ambient of 760 torr plus blood pressure mean of 100 torr, or a total of 860 torr).

13) Both the blood withdrawal syringe and the heparinized saline syringe should be operated by a single drive or have an interlock for position orientation.

14) The blood syringe must not be bottomed at termination of stroke but held at .035 to .050 inches from the bottom and held in place during the flushing stroke of the heparinized saline solution.

15) A positive restriction must be provided to prevent blood from entering flushing ducts or the leakage of flushing fluid into blood catheter during the non-operative period. The flushing holes should not exceed 0.3 mm I.D. The number and angle of entry are critical.

16) The valve is not to be affected by a 20 G shock load or random vibration test.

17) The heparin syringe for makeup solution to have positive travel control and connecting tube of small enough I.D. to restrict heparin flow to that of the heparin syringe actuation or positive shut off.

18) A thermistor or thermocouples are to be on the outside of the pulmonary artery and on the aorta.

19) There are two automated withdrawal and re-injection syringes required for taking samples, five minutes apart, every 6 hours from the pulmonary artery and aorta (catheters).

20) The dye-injection (0.1 mg/kilo of animal) syringe on vena cava catheter is to inject duplicate samples 5 min apart every 6 hours.

21) The flushing syringes on the left atrium, aortic, pulmonary artery, heparin saline dye solution injection and vena cava catheters should be activated every hour. A 2 ml max. flush of catheters (total) every hour (T/M this event as part of the schedule).

22) There is a requirement for a pressure sensor on each of the aortic, vena cava, pulmonary artery and left atrium catheters.

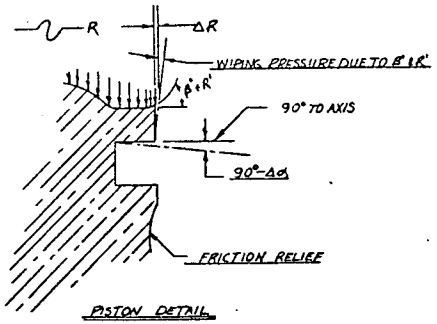
23) Densitometers (805 mμ and 660 mμ) for aortic and pulmonary arterial catheters are required.

24) The refractometer (805 mμ) is to be on the aortic catheters.

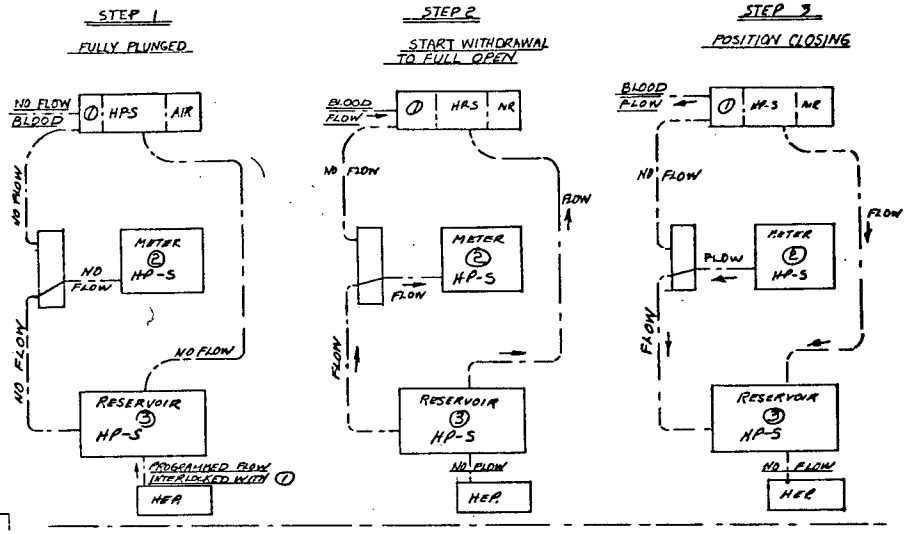
25) All devices should have a 60 day reliability, with a 90 day performance capability.

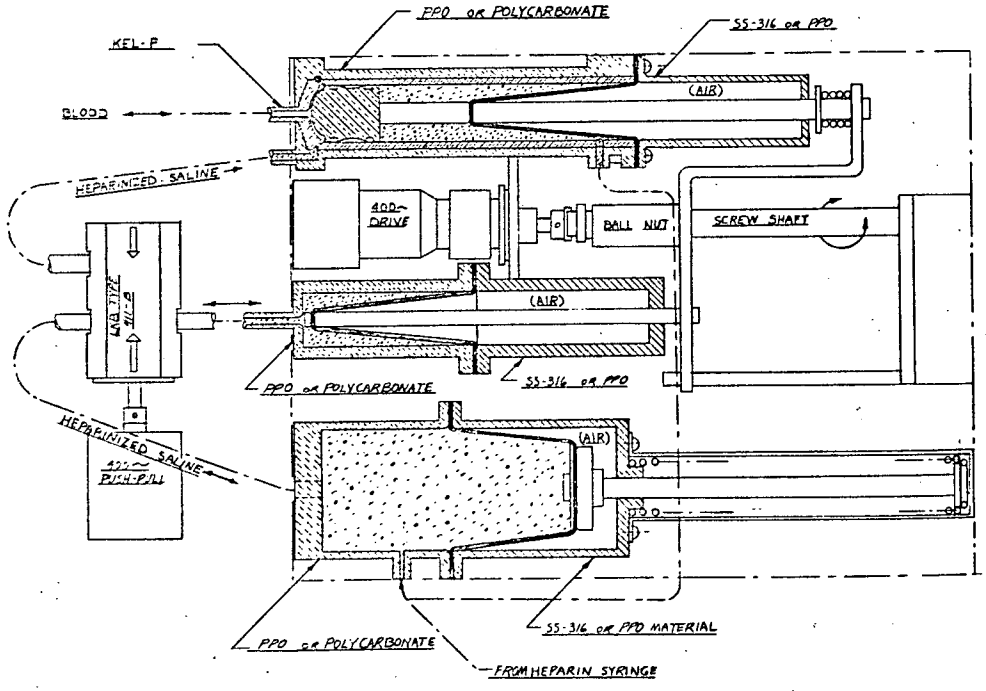
26) At no point should metal come in contact with blood.

27) All methods and materials of sterilization that come into contact with the blood must be capable of physiological integrity of the blood.



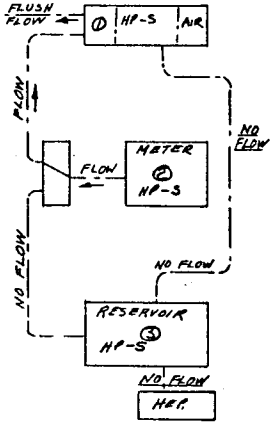
PISTON DETAIL





STEP 4

BLOOD SYRINGE CLOSED
HEPARINIZED SALINE FLUSH



UNIVERSITY OF CALIFORNIA
BERKELEY – APRL PROJECT

BLOOD WITHDRAWAL SYRINGE

DNG *AHS-2
DATED 25/4/67

Hemodynamics Subsystem Design Data for the 8.0 kg Pig-tailed Monkey.

Physiological Parameter		Mean Value	Dynamic Range Required		
			Max	Min	Accuracy
Respiratory Rate	(breaths/min)	34	70	0	± 1 breath/min
Heart Rate	(beats/min)	193	275	0	± 1 beat/min
Aortic Systolic Pressure	(torr)	+127	+300	0	± 1.0 torr
Aortic Diastolic Pressure	(torr)	+ 76	+160	0	± 1.0 torr
Aortic Pulse Pressure	(torr)	+ 51	+140	0	± 1.0 torr
Aortic Mean Pressure	(torr)	+100	+200	0	± 1.0 torr
Venous Mean Pressure	(torr)	0.00	+ 10	-10	± 0.1 torr
Left Arterial Pressure	(torr)	0.00	+ 10	-10	± 0.1 torr
Pulmonary Arterial Mean Pressure	(torr)	+ 16	+ 50	0	± 0.1 torr
Cardiac Output	(liters/min)	0.97	3.00	0	± 0.01 liters/min
Stroke Volume	(ml)	5.4	25.0	0	± 0.1 ml
Systemic Resistance	(dyne sec/cm^5)	8,505	40,000	0	± 100 dyne sec/cm^5
Left Ventricular Power	(watts)	0.216	1.000	0	± 0.01 watt
Pulmonary Resistance	(dyne sec/cm^5)	1,313	40,000	0	± 10 dyne sec/cm^5
Total Hemoglobin Concentration	(g/100 ml)	11.3	25.3	0	± 0.1 g/100 ml
Aortic Oxyhemoglobin Conc.	(g/100 ml)	11.0	25.0	0	± 0.1 g/100 ml
Pulmonary Artery Oxyhemoglobin Conc.	(g/100 ml)	11.0	25.0	0	± 0.1 g/100 ml
Aortic Oxygen Partial Pressure	(torr)	107	125	0	± 1.0 torr
Pulmonary Artery Oxygen Partial Press.	(torr)	37	100	0	± 1.0 torr
Total Blood Volume	(ml)	500	800	0	± 5 ml
Total Plasma Protein Conc.	(g/100 ml)	7.23	10.0	0	± 0.1 g/100 ml
Temperature, Aortic Wall	(°C)	37.5	45.0	25.0	± 0.1 °C
Temperature, Pulmonary Artery Wall	(°C)	37.5	45.0	25.0	± 0.1 °C

Addendum:

Parameter		Frequency of Measurement	Accuracy
Dye Concentration	(Injection Side)	2x 5 min apart, every 6 hrs	± 0.01 mg/ml
Amount of fluid	(Injection Side)	2x 5 min apart, every 6 hrs	± 0.1 ml
Catheter flush	4 catheters	1x each hour in addition to aorta fluid associated with C.O. determination	Not to exceed 2 ml total of heparine saline solution each flush cycle.

SECTION VI

REPORT OF THE APRL RESTRAINT SUBSYSTEM WORKING GROUP

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By way of introduction to the difficult subject of restraint the initial topic considered by this working group should set the tone for this report. This was the idea that a system of restraint which provided only minimal physical restriction, similar to the colony situation, would have the highest probability of maintaining a monkey in excellent physiological condition for a 90 day period. The obvious argument against such a system is that it would restrict the type and quality of physiological measurements to be made. Because discussion was raised as to the relative merits of this argument it is recommended that further consideration be given to this possibility.

An experimental approach, outlined in an appendum to this report, is offered as a stimulus to thinking on this topic.

Underlying these introductory comments is the possibility that as one decreases the animal's ability to move in whatever restraint system used the greater the chances of adversely influencing the measurements of interest and of impinging upon one of the inviolate requirements of the APRL experiment, namely the physiological well-being of the animal.

PAST EXPERIENCE WITH THE APRL RESTRAINT SYSTEM

Table 1 compares the number of animals successfully restrained in the couch to those animals which had to be removed due to physical breakdown. The numbers were collected from the animal record files and the PHAMOS reports and while these figures do not include all of the monkeys used over the years, they do constitute a large sample of the total.

Table 1. Summary of seated restraint experience with the pig-tailed monkey at EPL.

Continuous Days of Restraint	Total Animals Tested	Successful Animals	Breakdown Animals	Per Cent Failure
10	64	51	13	20.3
20	47	42	5	10.6
30	33	29	4	12.1
40	17	15	2	11.8
50	9	9	0	0
60	6	6	0	0
70	6	6	0	0
80	5	5	0	0
90	5	5	0	0

The decline seen in the "success" curve represents primarily removal from the couch due to experimental design or loss of catheter patency. While the fact that it is possible to restrain a monkey for a 90 day period with the present system, it is difficult to ascertain from the data what reliability is associated with this method of restraint. The number of animals restrained for 90 days must be greatly increased.

The "breakdown" data represent those animals which had to be removed from the couch because of chafing from the jacket, ulceration in areas of contact with the couch, or edema of the lower extremities. While the numbers are again relatively small, the data do suggest that 50% of all breakdowns occur in the first 10 days of restraint.

The principal problems associated with the restraining devices used in this and other laboratories are the development of chafing and pressure ulceration, the latter being the more pervasive. Of prime consideration here is the blood circulation to the areas under the greatest pressure. The animal's ability to move these areas provides a partial solution to this problem. However, some research on an immobilized monkey in order to determine the most satisfactory solution to this problem should be considered, such as the use of special materials to reduce pressure, special techniques of changing pressure in susceptible areas, heating, vibration, etc.. Finally, attention should be paid to how the restraint system will change once the weightless condition is established, and if this condition will create a new set of problems (or solutions!) to be considered.

THE EFFECTS OF RESTRAINT UPON THE VARIABLES OF INTEREST

The second major area of concern of this working group was a consideration of the physiological effects of restraint. Some of the possible effects gleaned from the PHAMOS reports and from the literature[1] were:

1. Cardiovascular deconditioning.
2. Changes in the excretion of:
    a. Calcium
    b. Phosphorus
    c. Nitrogen
    d. Creatine
    e. Creatinine
    f. Hormones of adrenal, parathyroid, and possibly the thyroid.

---

[1] The primary sources in the literature pertaining to the physiological effects of restraint are:
Forsyth, R. P. and R. Baireuther. Amer. J. Physiol., 212: 1461-1463, 1967.
Hoffman, R. A. et al. Aerospace Med., 693-698, 1968.
Mack, P. B. et al. Aerospace Med., 698-704, 1968.
Mason, J. W. et al. Amer. J. Physiol., 190: 429, 1957.
Pyke, R. E. et al. Aerospace Med. 704-708, 1968.

3. Changes in bone density.

4. Alterations in body temperature.

5. Changes in body weight.

6. Changes in blood plasma, i.e. plasma volume and plasma proteins.

Because of these effects, three questions are of future importance:

1. Are these changes of such a magnitude as to put the monkey in danger of not surviving the stress encountered in the experiment, e.g. acceleration and reentry?

2. What are the dynamics of these changes? Are they short or long term effects, biphasic, cyclic, etc., and most important what are the means and standard deviations of these changes?

3. What conditions will modify these changes, either to minimize or to make more predictable?

Because the answers to these questions are as yet unavailable, the following recommendations are made:

A. The present APRL couch system should be given further systematic testing to determine its reliability for a 90-day experiment. Reliability should be determined for normal as well as fully instrumented monkeys.

B. The physiological effects of restraint in the present system should be determined and means sought to eliminate deleterious effects. These effects range from the production of chafing and pressure ulcerations to the influences on those variables of experimental interest; e.g., hemodynamic function, nitrogen balance, etc.

It is clear that the major problem of restraint is not the mechanics of keeping the monkey from destroying the means of making the desired physiological measurements, but to do this in a monkey which must remain in an excellent physiological and psychological condition; i.e. a

willingness to interact with its environment to obtain adequate nutrition, to explore and manipulate, to seek some level of sensory input, to emit some level of motor activity, etc.

General Requirements of the Restraint System.

1. Whole body orientation must remain in one or possibly two alignments with respect to the surrounding structures, especially the monkey module, urinary, hemodynamic and fecal subsystem. This was proposed in McDonnell report F557 as a requirement and whether this is an immutable requirement should be determined. (TBD)
2. The restraint system must not produce detrimental effects to the monkey's health such as chafing, pressure ulceration, and edema of lower extremities. TBD - methods of reducing these effects, e.g. flexible foot rest, hand bars to assist the monkey to change body position, methods of reducing pressure points such as a dynamic restraint system which can be adjusted to various positions, etc.
3. Restraint should be sufficient to prevent the monkey from interfering with the module structure.
4. Design of the restraint system must be simple, maintainable, and compatible with the monkey module, nutrient, and environmental control.
5. Restraint system shall not impose additional loads on the monkey by requiring it to support elements of the restraint system or instrumentation components.
6. TBD - how closely the restraint system must fit the measurements of each individual monkey, and will all portions of the system

require the same degree of fit.

7. TBD - A method of specifying movement in terms of angles and/or measurements of various parts of the body so that a more accurate determination can be made of the amount of restraint needed so as not to unduly restrict the animal's movement.
8. General question - Because it has been mentioned that there may be differently instrumented monkeys in the final APRL experiment, are the requirements for the restraint system of such a nature that appropriate independent systems could be built, e.g. one to use with monkeys from which urine, feces, and LBNP will be analyzed, and another for monkeys where restriction of the upper body is necessary (hemodynamic and metabolic measurements)?

Acceleration and Reentry.

Problems associated with acceleration and reentry are in terms of the dramatic increase in contact pressures, vibrations, buffeting, and impact.

(TBD) the amount of support and restriction of movement of the various structures of the body, to increase areas of contact with the restraint system, to adequately distribute pressure points and to eliminate physical injury due to the head, arms, legs, or body trunk striking against the restraint system. In addition, catheters, etc. shall not be adversely affected by the restraint system under these conditions. If a close tolerance is required to eliminate movement, some means of adjusting the restraint system to accommodate the possible weight changes which might occur during pre-flight and/or during the flight.

Hemodynamics.

The problem associated with this subsystem is one of maintaining the integrity of the catheters and/or wires which exit through the posterior body wall.

Hands, feet, and body trunk are the major sources of worry. The couch system at the present time maintains integrity by the nylon jacket tied in place to the back of the couch which prevents the body trunk from moving in such a position as to block flow through the catheters and by restricting the feet by the lap guard. The main effect of this system other than maintaining the catheters is the fairly rigid restriction of trunk movement. (TBD) Would some other means of restraint allow trunk movement while meeting the intended requirements?

Metabolism.

The problem varies considerably with each proposed technique of making this measurement. The system which is under present consideration will not place any constraints upon the monkey's movement.

Nutrition.

Feeding system must be close enough to the monkey's mouth to allow minimal movement by the animal to come into contact with the nipple, i.e. the monkey must not have to strain to reach and make sustained drinking responses, but the spout should be far enough from the monkey to minimize play with the nipple. (TBD)

Activity and Body Mass.

Restraint system should be of such a nature to allow amount and type of activity and body mass measurements during all phases of the experiment. (TBD) how these measurements would be determined and what they would require of the restraint system.

Urine Subsystem.

Natural. Restriction of the lower body to the collection system.

Ureteral. The problem is to prevent hands, feet, and legs from inpinging upon the integrity of the catheters leaving each thigh. The present system depends upon the lap guard to prevent the hands from getting in contact with body areas below the waist and the legs from moving upward far enough to allow feet from damaging the catheters.

Feces Subsystem

Natural. Restriction of the lower body to the collection system.

Colostomy. The area of concern is the lower abdominal wall. This technique requires essentially the same constraints upon the restraint system as does the urine collection by the ureteral catheters.

LBNP

A suitable cuff must be placed around the animal's waist and the as yet to be determined garments and apparatus to create the reduced pressure around the lower half of the animal's body. Hands, feet and legs must be restricted so as not to break the seal necessary to maintain the reduced pressure. Feet and leg restriction appears to be similar to that needed to maintain the ureteral catheters and the feces collection system. The hands would require further restrictions, probably some method of restricting the hands from the upper waist area as well as below this area. (TBD)

AN INITIAL ENGINEERING TEST PLAN FOR APRL RESTRAINT DESIGNS

1.0 Introduction - The previous report of this work group was concerned primarily with the reliability testing and the physiological effects of any restraint system being considered for the APRL experiment. Because these questions are highly interrelated, it is felt that the information of most immediate importance is the physiological consequences of restraint. On the one hand, reliability of the restraint system is defined in terms of the severity of these consequences and once understanding of these effects is established increased reliability will be easier to obtain. On the other hand, the APRL experiment depends not only on a restraint system which will meet all of the requirements of the various subsystems as well as the forces encountered during acceleration-reentry, but also on a system which will not produce physiological changes of such a magnitude as to prejudice the determination of the effects of weightlessness. For these reasons the following test plan is proposed.

1.1 Scope - This document defines a 21 day test plan for the determination of the physiological consequences of any restraint device considered for the APRL experiment. A 21 day period is judged adequate to determine the direction of any physiological changes which may occur.

1.1.1 This Plan will be carried out under minimal restraint requirements for a 21 day period to determine the extent of physiological deterioration from the restraint system during this time period.

1.1.2 Minimal restraint requirements are defined as the minimum hardware necessary to ensure the monkey's confinement to the particular restraint system being tested, e.g. the couch requires a lap guard or its equivalent, the chair device requires neck and waist plates, the arm-shackle system requires only the arm shackles, etc.

1.1.3 Physiological deterioration will be determined by pre- and post-restraint examination.

1.1.4 This constitutes an initial test plan to establish the effects of the restraint system free from the influence of factors other than

the restraint device itself. If any device is found to cause extensive deterioration under this test then considerable alterations would be required before that system could adequately meet any of the APRL requirements.

1.1.5 If considerable individual subject variation is found in terms of the physiological measurements taken, the test would be repeated with an additional group of monkeys.

1.1.6 Once satisfactory results were obtained, a new test program could be established to include the APRL requirements to determine the extent of the interaction between these requirements and the restraint system.

2.0 Applicable documents

2.1 Forsyth, R. P. and Bairenther, R. Systemic arterial blood pressure and pulse rate in chronically restrained rhesus monkeys. Amer. J. Physiol., 212: 1461-1463, 1967.

2.2 Hoffman, R. A., E. A. Doxier, P. B. Mack, W. N. Hood, and M. W. Parrot. Physiologic and metabolic changes in Macaca nemestrina on two types of diet during restraint and non-restraint. I. Body weight changes, food consumption and urinary excretion of nitrogen, creatine and creatinine. Aerospace Med., 39: 693-698, 1968.

2.3 Mack, P. B., R. A. Hoffman and A. N. Al-Shawi. Physiologic and metabolic changes in Macaca nemestrina on two types of diets during restraint and non-restraint. II. Bone density changes. Aerospace Med., 39: 698-704, 1968.

2.4 Mason, J. W., C. T. Harwood and N. R. Rosenthal. Influence of some environmental factors on plasma and urinary 17-hydroxycorticosteroid levels in the rhesus monkey. Amer. J. Physiol., 190: 429, 1957.

2.5 Pyke, R. E., P. B. Mack, R. A. Hoffman, W. W. Gilchrist, W. N. Hood, and G. P. George. Physiologic and metabolic changes in Macaca nemestrina on two types of diet during restraint and non-restraint. III. Excretion of calcium and phosphorus. Aerospace Med., 39: 704-708, 1968.

3.0 Primate subjects

3.1 Six adult, male, pig-tailed monkeys *(Macaca nemestrina)* between 8-12 kg having had no previous history of restraint or other testing or surgical procedures (could be run in squads of three).

3.1.2 The monkeys shall be matched as nearly as possible with respect to anthropoidimetric measurements.

3.2 Six identical restraint devices with accompanying hardware will be used for the test (it would be less expensive to run in squads of 3 but obviously the test would take twice as long).

3.2.1 These restraint devices will be equipped to collect urine and feces.

3.2.2 The restraint devices should be made of material which allows visual inspection of the monkey with minimum manipulation of the animal.

3.2.3 The restraint system shall be placed in isolation booths which provide adequate ventilation, temperature, lighting, a means of observing the monkey without disturbing the animal, and a means of collecting urine and feces without entering the chamber.

3.2.4 Means of providing the monkeys with H_2O and food thereby circumventing contact with the animal.

4.0 Test procedure.

4.1 Pre-Restraint.

4.1.1 Body weight, food (Purina) and water intake records will be taken until satisfied that the animal's weight has stabilized.

4.1.2.1 The animal's diet will then be changed to the homogenate, D52.

4.1.2.2 This diet will be delivered in an identical manner to the restraint condition.

4.1.2.3 Intake and weight records will be taken until equivalences to the pre-D52 conditions are established.

4.1.2.4 Weights will be stable for at least one week prior to the restraint phase of the test.

4.1.2.5 Urine and feces will be collected for analyses during this week.

4.1.3 A comprehensive physical examination of the experimental primate will be made prior to being placed in the restraint device.

4.2 Restraint.

4.2.1 The animal in the restraint device will be placed in the isolation booth where identical conditions of light, ventilation, temperature level of external sound, etc., will be maintained for all of the experimental animals.

4.2.2 Light-dark cycles - 0600-1800 On
1800-0600 Off

4.2.3 Food will be available only during the light cycle.

4.2.4 Urine and feces will be collected continuously from the restrained monkeys. These must be removed from the isolation chambers without disturbance to the animal at 24 hour intervals.

4.2.5 Visual observation from several angles will be possible from outside the isolation chambers, allowing one to observe the animal's general condition, food and H_2O intake, etc. without disturbing the monkey.

4.2.6 Weekly inspections of the animal's general condition. Noting such things as position in the restraint device, condition of callosities, skin around contact areas. Body weights will be taken if possible. This will be accomplished with minimum disturbance to the animal.

4.2.7 Daily calculation of food and H_2O intake by the level of diet remaining in food reservoirs.

4.2.8 Routine checks shall be made on the feeding devices to insure proper operation.

4.3 POST RESTRAINT.

4.3.1 The second comprehensive physical examination will be made at the end of the 21 day restraint period.

4.3.2 Recovery will be studied for the two weeks following restraint with a physical examination at the end of each week.

5.0 Determination of Well-being. To satisfy this requirement it is necessary to have a complete physical examination of the monkey's health and physiological condition before as well as after the restraint period to assess the amount of deterioration due to 21 days of restraint.

5.1 Body weight.

5.2 Food and water intake.

5.3 Condition of skin and callosities with major concern in areas of the body where contact is made with the restraint system.

5.4 Urine constituents -- taken prior, during, and post-restraint -- to be specified.

5.5 Blood constituents -- taken prior to and following the 21-day test period -- to be specified.

5.6 If instrumentation can be developed in time, an exercise test measuring heart rate and O_2 consumption to determine efficiency under some mild physical stress conditions will be included in the test procedure.

5.7 General description and comments will be noted throughout the entire test, i.e. use of legs, home cage behavior, etc.

6.0 Support.

6.1 Personnel.

6.1.1 Veterinarian - 1 - to make initial and final physical examinations.

6.1.2 Physiologist - 1 - to oversee the integrity of the test and insure proper inspection of animals, maintenance of records, etc.

6.1.3 Technicians - 2 - part-time to maintain the monkeys, record food and water intake, process urine and feces, to observe the animals in the restraint devices, etc.

6.1.4 Physiological psychologist - 1 - to work in collaboration with the physiologist during the exercise test.

6.2 Testing facility. Must be adequate to allow animals to be away from daily activities of the laboratory, e.g. one 8x8x8 testing chamber. A small physical examination room, equipped with examination table and exercise test apparatus. The necessary equipment to process and store urine and feces collections. Adequate space near the testing chamber for programming equipment for lights and food/water. Storage for the monkey diets.

7.0 Conclusion.

7.1 This test plan should provide the necessary minimum information from which to begin the design of an APRL restraint system. Attempting to anticipate the results and conclusions:

Results	Conclusions
Negative - severe deterioration	Reject system or greatly modify, with the type of deterioration in mind, followed by a retest.
Positive-minimum deterioration	Add APRL subsystem requirements step by step followed by retesting.
Mixed	Modify and retest or add requirements to see if greater deterioration takes place.

7.2 The following is set forth as a first approximation of an overall testing strategy for the difficult area of restraint.

Phase I. Assessment of Restraint Principles - testing of principles which have minimal physiological consequences in addition to meeting APRL requirements.

Phase II. Restraint System Integration - the testing of systems which have incorporated viable principles previously tested.

Phase III. Reliability Testing - the testing of any system to emerge from phase II.

TESTING STRATEGY FOR THE RESTRAINT SYSTEM*

Restraint Principles-Phase I.	Restraint System Integration-Phase II.	Reliability-Phase III.
Jan Feb Mar Apr May	June July Aug Sept Oct	Nov Dec Jan
1. Couch [21] - [x] -IA+R- [21] -R- [21]	System A. [21] -IA+R- [21] -R- [21] - [x]	
2. Chair [21] -IA- [21] -R- [21] - [x]	System B.	
3. Arm Shackle [21] - R - [21]	System C.	System I. [90-120 day test]
4. Etc.		
5. Etc.		System II.
6. Etc.		

[21] = 21 day test plan

[X] = Rerun of the 21 day test plan - e.g. perhaps due to large within subject variability.

IA = Interim activity - development of techniques to handle small problems encountered in the previous test, e.g. new material for the butt plates.

R = Addition of the APRL requirements.

* Testing under the various phases would be carried out as material, personnel, animals, and facilities become available.

SECTION VII.

REPORT OF THE APRL FECES SUBSYSTEM WORKING GROUP

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1. Introduction.

This report presents an engineering discussion of the Phase II Task A study of the Feces Subsystem as it exists currently. Additions and deletions will be made as progress of the engineering-biology interface demands.

Study Approach - Technical requirements will be derived from the scientific guidelines furnished by the biologists. These data will be used for analyses and design to develop a configuration base line for the concepts. Alternate approaches and concepts will be studied to avoid uncertain state-of-the-art development or techniques. Trade studies will be performed in collaboration with the scientific staff to ensure that the optimum base line concept is chosen using commercially available flight qualified hardware wherever possible.

Program Approach - The engineering approach to the development will be to safeguard the scientific data validity of the system, and to meet fully and effectively its technical requirements embodied in a fail safe design. The development of engineering hardware is not the purpose of this program. It is the biological experiment that is most important and its needs determine the guidelines.

2. Scientific and Technical Integration Plan.

To attain the primary objectives of the Feces Subsystem, a proposed operational plan has been developed. This defines by task the specific areas and where a mutually effective team participation is required. A further expansion of the effort is included in Task Descriptions, grouped as follows:

Task Descriptions

Reliability, Analyses and Criteria

System Engineering and Integration

Review and Summary

2.1 System Engineering and Integration - System engineering and integration shall be conducted through close collaboration and coordination between all members of the APRL team. To ensure systematic development of the Feces Subsystem, the engineering process shall be based on the data indicated in this document.

2.2 Reliability Analyses and Criteria - The reliability concepts will be blended with the conceptual studies through the close association of reliability and design concepts. As Phase IIA progresses, a reliability value will evolve based upon trade studies and system development.

The design review activity will be continuous to assure a high reliability and confidence level in the final design. It also provides an opportunity to coordinate ideas between the engineering elements of the working team, and provides the means for carrying out reliability disciplines into each design phase.

2.3 Task Descriptions - Engineering will provide the support and services necessary to accomplish the following effort.

2.3.1 Liaison - Engineering will maintain a close technical liaison with the scientific staff to assure an optimization of the proposed items of work.

2.3.2 APRL Systems - To facilitate the analyses of the design concepts, it is necessary to consider all interfacing subsystems. Appropriate techniques will be used to ensure the orderly development

of base line criteria and to study the interaction between the Feces Subsystem and other subsystems. Those subsystems having the closest interface are the Bio-Module, Experiment Envelope, and Environmental Control Subsystem.

2.3.3 Technical Documentation and Reports - Documentation for this study effort will be provided to define a Feces Subsystem configuration base line design concept and performance criteria. Analysis summaries and configuration study drawings will be provided, as appropriate, to substantiate and further define the concepts selected. Specific items for submittal will be:

Feces Subsystem design and criteria specifications.

Definition of Feces Subsystem configuration base line design concept, with summarized analyses and configuration study drawings.

2.3.4 Master Schedule.

2.4 Review and Summary - The results of Phase IIA will be the consequence of considerable effort, and will be necessary for Phase IIB development and progress. As such, they are essential products generated by certain activities or functions under certain boundary conditions and constraints.

2.4.1 Boundary Conditions and Constraints - The boundary conditions and the constraints that serve to direct The Feces Subsystem base line include:

Requirement for scientific validity of acquired data.

Requirement for the scientific integrity of the complete subsystem.

Requirement for the Feces Subsystem to operate automatically and continuously for 60 days, but with the capability for 90 days in the unattended mode.

Requirement for the Feces Subsystem to be ultimately suitable for a 60-day space mission.

Requirement for a short term reentry feces subsystem.

2.4.2 Functions - The various functions which will be performed to define the preliminary base line of the Feces Subsystem will be analytical, evaluative, and studied, in nature. These functions, which may have more than one output as a product, include:

The acquisition of information and data pertinent to design.

Assessment of the present state of the art hardware components to be used.

Trade study effort to determine an optimal design concept.

Evaluation of component suitability in terms of performance characteristics.

Evaluation of component suitability in terms of experiment procedure compatibility.

2.4.3 Products - The products include:

Presentation of Feces Subsystem design concepts.

Definition of general engineering criteria essential for design of the Feces Subsystem.

Evaluation of the compatibility between the monkey/subsystem interface.

Circumscription of the major problem areas.

Definition of subsystem preliminary base line design.

3. Physiology/Engineering Interface.

The APRL is an orbital laboratory for the study of environmental physiology. The research objective is the investigation of physiological effects of weightlessness.

3.1 Feces Subsystem Function - The term Feces Subsystem function is intended to cover the various aspects of handling, collecting, and storing activity that will be measured. These include not only the physiological characteristics of the excretion action of the feces biological subsystem, but also include the estimation of the degree of liquid and gas expelled and of the consistency of the feces as it leaves the animal.

During the continuous period of days in the weightless state, the normal passing of excrement is not on a predictable hourly time period. It therefore becomes important to establish the time of the action and amount of feces qualitatively that has occurred.

3.1.1 Feces Output - The outflow rate, termed the feces output, is found to vary from 0 to 50 ml/min depending upon the physiologic state of the monkey. At any particular time, the output value is determined by a number of reflex processes.

During Phase I several methods studied for the continuous measurement of feces output led to the selection of the colostomy as one technique available. In this method, an opening was made in the abdominal wall for the expulsion of the feces. The problems of tissue shrinking and bag attachment has not been satisfactorily solved. The attachment of a device to the anus by means of a flexible cable through a tubing inserted in the pelvic bone showed some possibilities but was not satisfactory. The use of bone screws and rivets were tried and proved to be equally unsatisfactory.

A procedure has been planned for the attachment of a polyvinyl ring onto the external tissue of the monkey at the anus. This ring will be attached by adhesive and a determination made as to its time and adhering qualities.

The time and amount of feces can then be measured directly by means of a sensing transducer which may sense changes in optical density, electrical resistance, capacitance, pressure, or volume. A suitable method for actual collection, time identifying, freezing and storage has not been decided upon. The only possibility offered to date is the "sausage" machine concept in the APRL Design Concept Book.

The goal for the Phase II design effort is to make output determinations and a means of collecting and packaging same. The automated feces output apparatus will contain sufficient storage capability for this purpose. From such data it will be possible to define any changes which may occur in the general level of the feces output.

4. Subsystem Design Concept.

The Automated Feces Subsystem will be designed to comply with the requirements as specified by the scientific staff based on the initial design work accomplished by the conceptual design book for APRL but will not be restricted to the limited design concept.

The function of this subsystem is to collect, identify timewise, and store the feces with minimal physiological effect on the monkey.

5. Requirements.

I. Establish dynamic range of fecal production and content on a standard diet for:

A. Determinations to be made on 6 monkeys for 90 days:

1. Frequency of defecation
2. Consistency
3. Amount (weight wet and dry)
4. Hydrogen ion concentration

B. Evaluate the determinations under A with 6 monkeys when:

1. Free in cage
2. In restraint with surgery
3. In restraint without surgery

C. Time and personnel for experiment

1. Technical personnel requirements: 10 man hours/day/ for 6 monkeys

D. Equipment for fecal study

1. Freeze
2. Freeze dry
3. Warm air dry
4. Chemical preservation

II. The experimental model (the monkey)

A. Anal collection

1. With and without anal cast

B. Colostomy with sub peritoneal abdominal ring (six weeks for each preparation)

1. Necessity for determining engineering and biological characteristics with Dow Corning Institute for Aid to Medical Research (12 months)
2. Consultation with colo-rectal specialist
3. Total manpower TBD

III. Fecal chemical analyses have been discussed and whether they should be included in this experimental design or under "Nutrition" is undecided at present.

IV. Status of flatus

A. Design experiment on the proposed APRL diet for 30 days with and without surgery to determine:

1. The total quantity flatus/24 hours
2. The individual components
3. Time and manpower TBD

B. Evaluate available methods and data from Biosatellite III and Man Space flight on flatus management.

SECTION VIII.

REPORT OF THE APRL URINE SUBSYSTEM WORKING GROUP

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The following report considers two topics: the Urine Collection Subsystem, which includes the urine line from the monkey catheter through storage and preservation, and on-board biochemical analyses.

A. THE URINE SUBSYSTEM

1. Dead Volume.

Establish approximate length and inside diameter of the extension on catheter tubing leading from monkey catheter to urine analyzer. The guidelines should be the desirability for smallest "dead volume" between the monkey interface and "analyzer". Also the inside diameter of the urine line should be uniform and free of objects which interfere with flow. If the G. E. UTA is employed, the inherent "dead volume" of the transport device will have to be added to the "dead volume" of the interconnecting length of tube.

2. Select-ion Electrodes.

Sense with "in line" measure the activity of the following five ions:

a) H^+

b) Ca^{++}

c) Na^+

d) K^+

e) Cl^-

The Select-ion electrodes should have their sensing element built in to conform with the contour of the tubing, and not projecting or occupying space in the lumen of the urine tube.

The section of the urine line containing the Select-ion electrodes should constitute an independent portion of the total urine line and should be coupled in just prior to integrating the whole urine subsystem. This is because calibrations, standardization and adjustment with known fluids could best be checked out outside the spacecraft, and inserted just prior to final assembly of the urine subsystem.

3. pH Adjustment.

The pH adjustment should be accomplished as part of chemical preservation during packaging. Since there is no real pH at which all desired urinary constituents will be equally well preserved for prolonged periods, the titration to a specific pH does not necessarily solve all problems, but complicates things considerably. Also the pH adjustment to any value prior to entering the analyzer is not a real requirement in the present subsystem even if the urine is somewhat alkaline. The total calcium (if affected by high pH) can then be analyzed readily in the preserved sample for that period in the laboratory. Also calcium ion activity is measured independently upstream.

Instead of an elaborate pH adjust system, use can be made of an acid such as benzoic acid or boric acid together with a bacteriostatic agent such as an oxide of mercury or some other mercurial salt. The resulting pH should be 5 to 6. This would appear to be adequate and more desirable than titration with mineral base to raise the pH and titration with mineral acid to lower pH, which would require elaborate and complicated titration systems.

Also:

1) Addition of an organic acid or boric acid and mercury oxide in

solid form would not change the urine volume and would not affect or interfere with the determination of all desired constituents.

2) The packaging containers can be charged with above crystals prior to assembly or perhaps impregnated with them (so can perhaps the whole urine line and sanitary system).

3) The diffusion of even a trace of mercury is sufficiently bacteriostatic.

4) The above agents are not volatile and thus impart no toxic vapors.

4. Packaging

Based on (1) laboratory experience that about 50 cc of urine is adequate for all desired urinary constituents, (2) that urine excretion can normally vary up to 110 cc per 3 hour period, and (3) the total volume is already measured and known, the selection of a packaging container should be based on a minimal volume of 50 cc and a maximum volume of 110 cc. In case of urine volume in excess of selected package volume, it should bypass into "Dispose".

5. Preservation

It has been well established in a number of studies, that chemical preservation alone will not preserve urine for any length of time (probably less than 14 days). Also, while chemical preservation may benefit one or more constituents, it may destroy others. Therefore freezing of stored samples appears to be the most feasible approach. The freezing temperature should not be warmer than -20°C. Lower temperatures would be more satisfactory.

A very important factor in storage even at low temperature is drying of the sample. Therefore precaution must be taken to avoid permeable

materials in the construction of the packaging containers.

Freeze-drying is perhaps the best method of preserving urine for 100 days. However there is one major disadvantage in freeze-drying (besides its considerable complicity in space flight), namely in that the individual 3 hour volumes of urine will vary considerably. Thus in reconstitution, considerable errors may be introduced. Besides not knowing *a priori* the volume to be freeze-dried, it might be difficult to design a freeze-drying flask to efficiently treat a 1 cc and a 100 cc volume. Also freeze-dried urine is extremely hygroscopic and unless it is maintained in an absolutely dry state, it may become "gummy" and deteriorate.

B. ON-BOARD BIOCHEMICAL ANALYSES

Biochemical analyses on a real time basis are most desirable for at least three main reasons:

1) The constituents are not degraded or changed.
2) The physiological status of the animal can be assessed more readily.
3) In case of failure of the preservation and storage system of the urinary specimen or failure of recovery, scientific data are not lost.

For this reason, it is obvious that the more constituents that can be analyzed in flight, the more scientific data are immediately available and the sounder the experiment.

The following six constituents are recommended for development in flight analysis:

1) Calcium
2) Creatinine

3) Creatine

4) Urea

5) Phosphate

6) Glucose

The analytical procedures for above constituents are relatively simple and require few reagents.

In any quantitative chemical analysis certain mechanical functions must be carried out with utmost precision in order to minimize the ultimate overall error.

1) Sampling - If a sampling device has an absolute error of ± 1% and a 100 microliter is taken for analysis, then a ± 1% error will result due to sampling alone. However if a 10 microliter sample is taken then the error becomes ± 10% due to sampling alone.

2) Dispensing - The addition of reagents must be done with a high degree of precision in reproducibility. Otherwise the cumulative total volume may vary and thus produce an error. Colorimeter procedures are based on having identical final volumes for standards blanks and unknowns.

3) Mixing - Unless the reagents and sample are rapidly and thoroughly mixed the expected reaction will not go to completion in a specified time interval. Complete mixing of reagents even in conventional vessels in the laboratory is a function of the viscosity of the liquids, shape of vessel and reactivity. Inadequate mixing and "dead space" produce "drift" and large errors. These problems and errors can be magnified considerably

when using small volumes, and in capillary containers. In absence of gravity, as in space, to assure proper mixing of fluids of varying concentrations of solutes is still a problem more serious than at 1 G.

4) Cleaning - Much time is normally spent in the laboratory to prepare uncontaminated vessels for analysis. Disposable vessels can be used only to a certain degree. Aliquoting equipment such as in sampling and dispensing pipets, and cuvettes are rarely uniform and therefore not interchangeable. Therefore proper cleaning must consist of removing all interfering substances. This in turn requires application of special cleaning solutions followed by rinsing with copious amounts of water. In the laboratory this presents no problem; in space it does.

In the JPL analyzer many errors can be attributed to lack of understanding of the importance of the above described procedural functions.

To prevent this shortcoming in the future, engineering concepts must take these functions into consideration. Before "freezing" any design, they must be laboratory tested.

There is presently under advanced development a radically new system of automatic analyses. This is the DuPont "Automatic Clinical Analysis" system. It is recommended that this system be seriously considered for adaptation to in-flight analyses for the desired urinary constituents. Following is a summary of operation of the DuPont system.

In the DuPont ACA system the reagents for each test are packaged in a special kit or pack which also serves as the reaction chamber and test cuvette for the photometric analysis. The packs are produced under

carefully controlled conditions to insure high quality and correct reagent quantities. Packs for certain types of tests contain individual disposable chromatographic columns to isolate specific constituents or molecular weight fractions.

A separate pack is used for each test performed on a sample. Each pack contains both the test name for convenient operator identification and binary code to instruct the analyzer. The technologist programs the analyzer by inserting the appropriate pack or packs behind each sample cup in the analyzer input tray.

The analyzer automatically injects the exact amount of sample and diluent into each pack in succession, mixes the reagents, waits a preset amount of time, forms a precise optical cell within the transparent pack walls, and measures the reaction photometrically. These operations are controlled and monitored by a built-in, solid-state, special-purpose computer and are performed under precisely regulated conditions within the instrument. The computer calculates the concentration value for each test and prints out a separate report sheet for each sample. This report contains all the test results on that sample along with the patient identification. The used test packs are discarded automatically into a waste container.

At present about six companies in the United States manufacture automatic analytical equipment. Each of their systems has some useful features. However the DuPont system appears most complete. It might also be possible to explore the possibility of combining some of the advantages in each system and incorporate it into one analytical unit.

Following is a suggestion of chemical method for on-board analysis:

Calcium - Method of Grunbaum and Pace. In this procedure calcein

is added as a fluorescent indicator and titration with EDTA is continued to the disappearance of fluorescence. In this manner the dynamic range for calcium concentrations should be large and linear.

Creatinine - Same method as in JPL analyzer but change quantity of reagents in order to use an optical cell (cuvette) of larger depth.

Creatine - Same as creatinine but heat with sulfuric acid prior to reaction with alkaline picrate.

Urea - Adapt the method of P. J. Geiger. This procedure utilizes p-dimethylaminobenzaldehyde and is suitable for automated equipment.

Phosphate - The method of Grunbaum and Pace should be modified to include a stable reducing agent for molybdenum.

Glucose - Adapt the method of Grunbaum and Pace, using the anthrone reagent.

Above methods, except for calcium, require light emission of 435, 490 and 660 mμ wavelengths.

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2. Geiger, P. J. Microchemical Journal.

DEVELOPMENT TEST PLAN

A. Monkey-catheter Interface

1. Develop methods to test and qualify silicon ivalon ureteral catheters of various sizes for the following characteristics:
   a) Sterilization
   b) Storage (retention of original properties)
   c) Pressure testing
   d) Cleaning procedures
2. a) Prepare six (6) monkeys by surgical ureteral catheterization and follow experiment for at least 90 days.
   b) Make periodic checks for urine sterility, pH and qualitative measurements, such as blood, glucose and protein.
   c) Make periodic checks in blood for NPN or urea.
3. Manpower:
   a) Development - 1 engineer and 1 biologist, 90 days each
   b) Shop support - 180 man days for fabrication and 90 man days for maintenance and set up.
   c) Testing
      1) Six surgeon days
      2) Three animal caretaker-technicians, 90 days each and 1 laboratory technician, clinical type, 90 days.
   d) Make available 6 UCB type couches, 6 automatic tilt barrels with fraction collectors, and 12 restraint garments.

B. The urine transport line (excluding analyzer)

1. Establish preliminary schematics and dimensions to show the following:

   a) Length of urine line including urine transport assembly

   b) Internal diameter

   c) Various subsystems, such as urine transport assembly, ion sensing, analyzer, and storage

   d) Materials (for compatibility with urine)

   The following guidelines are suggested:

   a) The urine volume between the monkey ureters and analyzer and storage must not exceed 50 ml (approximately the equivalent of a 3-hour output)

   b) The urine temperature should remain 35°C $\pm$ 2°C

   c) Urine line to remain free of bacteria; e.g., by use of UV irradiation

   d) Retain uniform lumen and avoid "dead-spaces" (to prevent stagnation)

   e) Back pressure of urine should not exceed 5 torr

   Manpower and time, mostly engineering TBD.

2. Select ion sensing.

   a) Design and build a breadboard model to accommodate Select-ion electrodes for H^+, Ca^{++}, Na^+, K^+, and Cl^- and test for:

      1) Sensitivity limits - concentration range for each ion

      2) Specificity - in mixtures

      3) Stability - length of time electrode will retain original properties

4) On line calibration - occasional calibration with known solutions must be possible

5) Linearity - establish at which concentration ranges the readout is a linear function of concentration

6) Length of cable - between electrodes and pH meter. Establish if there is a drop in sensitivity with lengthening of cable.

7) Sensitivity as a function of common reference

8) Sensitivity as a function of continuous flow

9) Sensitivity as a function of diminishing volumes of fluid

10) Perform tests with wide range of urines from man and monkeys

11) Adapt electrodes to uniform size - at least the sensing portion of electrodes.

12) Repeat and test (1) through (11) with electrodes and monitoring systems from one or more manufacturers

b) Manpower - engineering support TBD
shop support - TBD
1 technician - 6 months

3. Preservation of Urine

Refer to Urine Working Group report of 25 November 1969 and plan a lab-bench experiment.

a) List and evaluate possible materials for storage and preservation of urine.

b) Establish container configuration for urine storage.

c) Plan experiment (establish parameters) to evaluate the urine preservation qualities of (a) and (b) using:

1) Freezing without additives*

---

* Boric acid, benzoic acid, mercuric iodide or mercury oxide or any combination of these.

2) Freezing in presence of suggested additives

3) Additives without freezing

4) Freeze drying

5) Evaluate various additives for the purpose of quantity requirements for maintenance of bacteriostasis and pH between 4.5 and 6.5

6) Use pseudomonas infected urine to study effectiveness of additives

7) Continue periodic evaluations from time zero to one year

d) Manpower and time -- 2 laboratory technicians, one year each, occasional engineering consultation.

e) Availability of two freezers, at -20°C and at -55°C.

C. Analyzer

Recruit a special working group to establish general criteria for on-board chemical analysis for urinary constituents.

Phase 1 a) Discuss the number of urinary parameters to be measured

b) The order of their importance

c) Chemical complexity

d) Methods of analysis

e) Maximum permissible errors

Phase 2 a) Engage appropriate engineering talent to discuss feasibilities

b) Manpower and time requirement TBD

SECTION IX.

REPORT OF THE DATA HANDLING SUBSYSTEM WORKING GROUP

Neil M. Huber, Chairman

N. Burwell G. Taylor, Secretary

Jens E. Hansen

Arthur M. Kodama

Donald F. Rahlmann

Jack H. Wilmore

The Data Handling Subsystem Working Group has directed its efforts towards determining precisely the characteristics and numbers of data that APRL is intended to generate. Figs. 1-5 show the data sampling sequences which might be expected in a flight experiment.

It is evident that certain data numbers and characteristics still need to be determined, and that the personnel required to determine them are the appropriate personnel of the other Working Groups. The function of this Working Group will be the coordination of all data handling, once generated.

The data-handling system recommended by this Working Group consists of two parts: the recording system, which is as mentioned an immediate need; and the digital computing system, which presumably will be an ultimate need for the summarization and analysis of the recorded information. The computer system will probably consist of existing University of California computer equipment, and will not be purchased by the EPL.

The recording system includes standard laboratory analog recording equipment, e.g. strip-chart recorders, in addition to the digital tape-recording equipment necessitated by the NASA standards mentioned in the previous report, to permit comparison of the fidelity of multiplexed and digitized data with data that have been recorded directly in analog form.

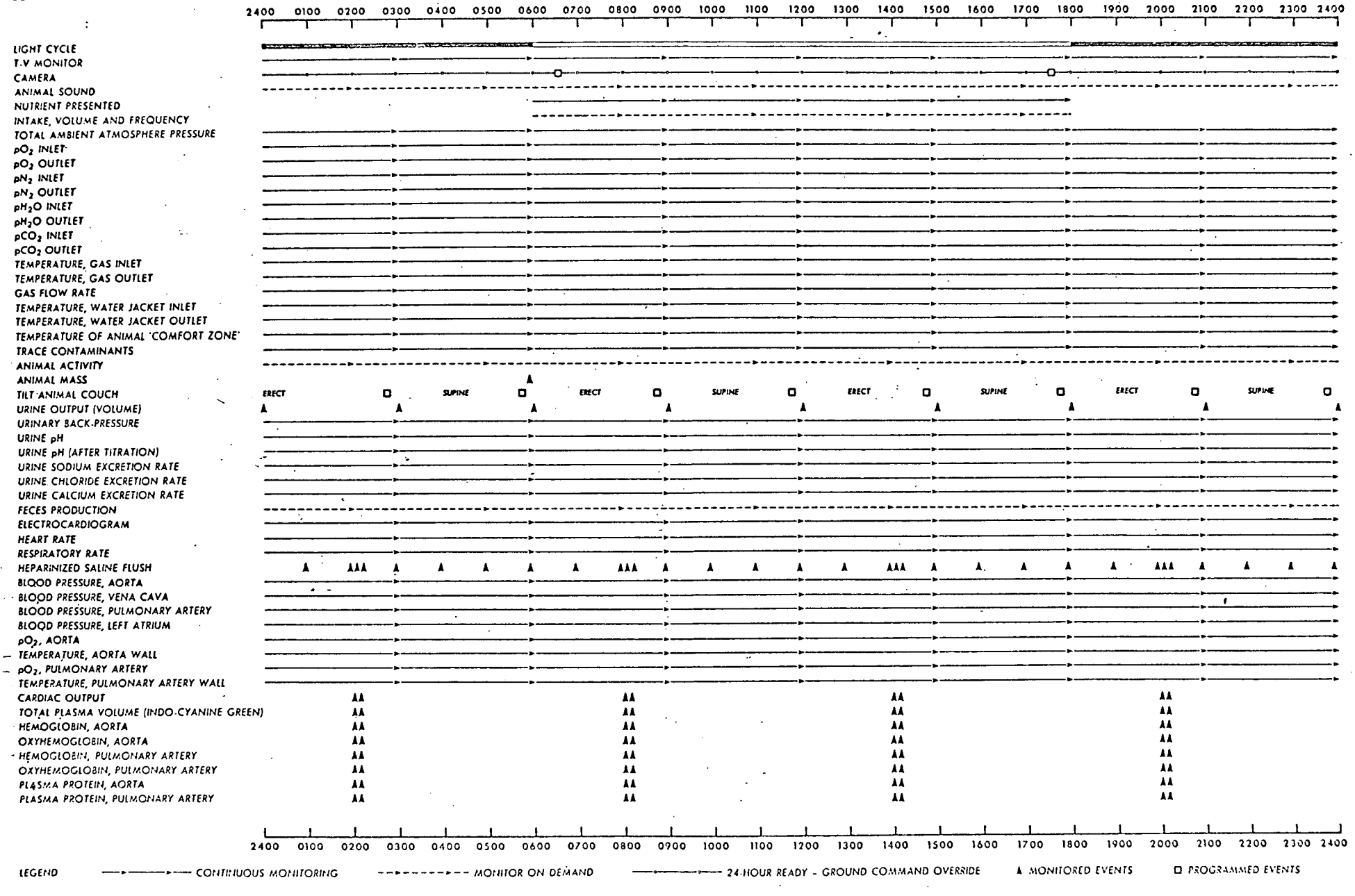
The digital tape-recording system will probably cost minimally $50,000.

The components of the recording system are all off-the-shelf items. The complete system, however, will be custom-designed specifically for the needs of the APRL project. Because the various components are produced in great variety by a number of manufacturers, the system should be designed on a contract basis by a data-systems consultant.

Engineering the system will probably require minimally three months and acquisition of a working system can probably take six months.

GROUND

1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LIGHT CYCLE
T.V MONITOR
CAMERA
ANIMAL SOUND
NUTRIENT PRESENTED
INTAKE, VOLUME AND FREQUENCY
TOTAL AMBIENT ATMOSPHERE PRESSURE
pO_2 INLET
pO_2 OUTLET
pN_2 INLET
pN_2 OUTLET
pH_2O INLET
pH_2O OUTLET
pCO_2 INLET
pCO_2 OUTLET
TEMPERATURE, GAS INLET
TEMPERATURE, GAS OUTLET
GAS FLOW RATE
TEMPERATURE, WATER JACKET INLET
TEMPERATURE, WATER JACKET OUTLET
TEMPERATURE OF ANIMAL 'COMFORT ZONE'
TRACE CONTAMINANTS
ANIMAL ACTIVITY
ANIMAL MASS
TILT ANIMAL COUCH
ERECT
SUPINE
URINE OUTPUT (VOLUME)
URINARY BACK-PRESSURE
URINE pH
URINE pH (AFTER TITRATION)
URINE SODIUM EXCRETION RATE
URINE CHLORIDE EXCRETION RATE
URINE CALCIUM EXCRETION RATE
FECES PRODUCTION
ELECTROCARDIOGRAM
HEART RATE
RESPIRATORY RATE
HEPARINIZED SALINE FLUSH
BLOOD PRESSURE, AORTA
BLOOD PRESSURE, VENA CAVA
BLOOD PRESSURE, PULMONARY ARTERY
BLOOD PRESSURE, LEFT ATRIUM
pO_2, AORTA
TEMPERATURE, AORTA WALL
pO_2, PULMONARY ARTERY
TEMPERATURE, PULMONARY ARTERY WALL
CARDIAC OUTPUT
TOTAL PLASMA VOLUME (INDO-CYANINE GREEN)
HEMOGLOBIN, AORTA
OXYHEMOGLOBIN, AORTA
HEMOGLOBIN, PULMONARY ARTERY
OXYHEMOGLOBIN, PULMONARY ARTERY
PLASMA PROTEIN, AORTA
PLASMA PROTEIN, PULMONARY ARTERY
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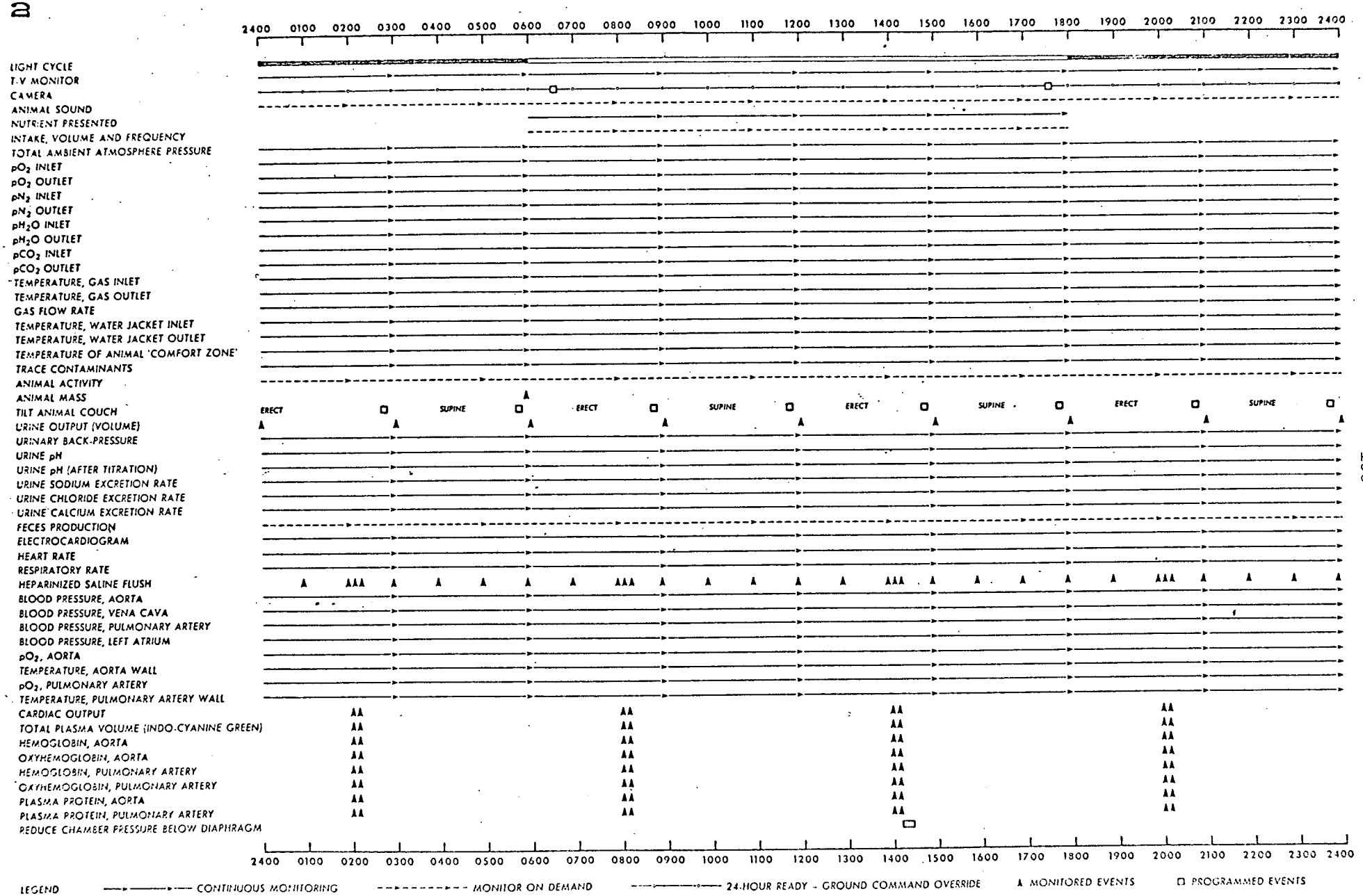
LEGEND
CONTINUOUS MONITORING
MONITOR ON DEMAND
24-HOUR READY - GROUND COMMAND OVERRIDE
MONITORED EVENTS
PROGRAMMED EVENTS

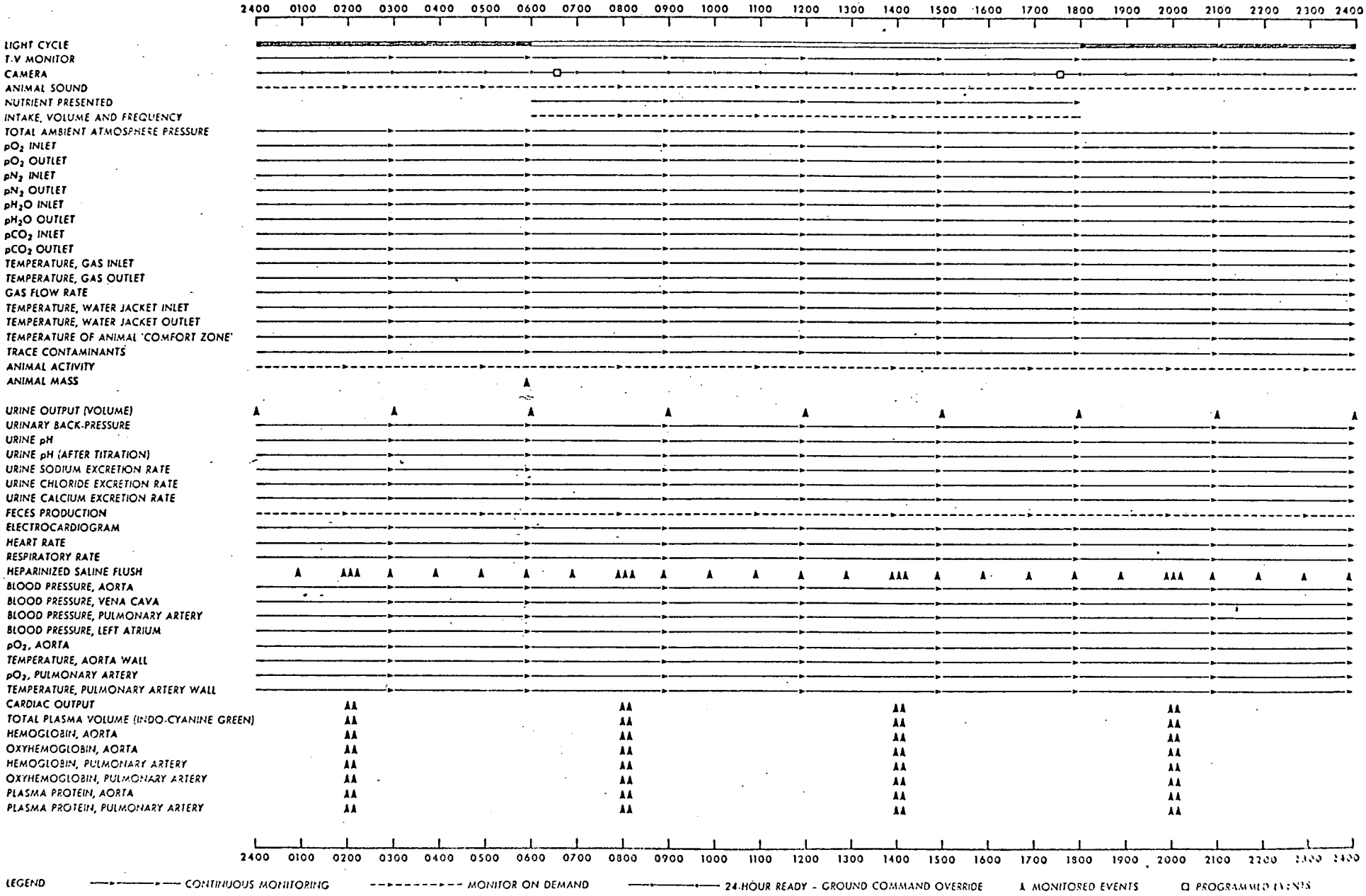
GROUND WITH EBNP

2



FLIGHT

3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T-V MONITOR
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INTAKE, VOLUME AND FREQUENCY
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pN2 OUTLET
pH2O INLET
pH2O OUTLET
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TEMPERATURE, GAS INLET
TEMPERATURE, GAS OUTLET
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PLASMA PROTEIN, PULMONARY ARTERY
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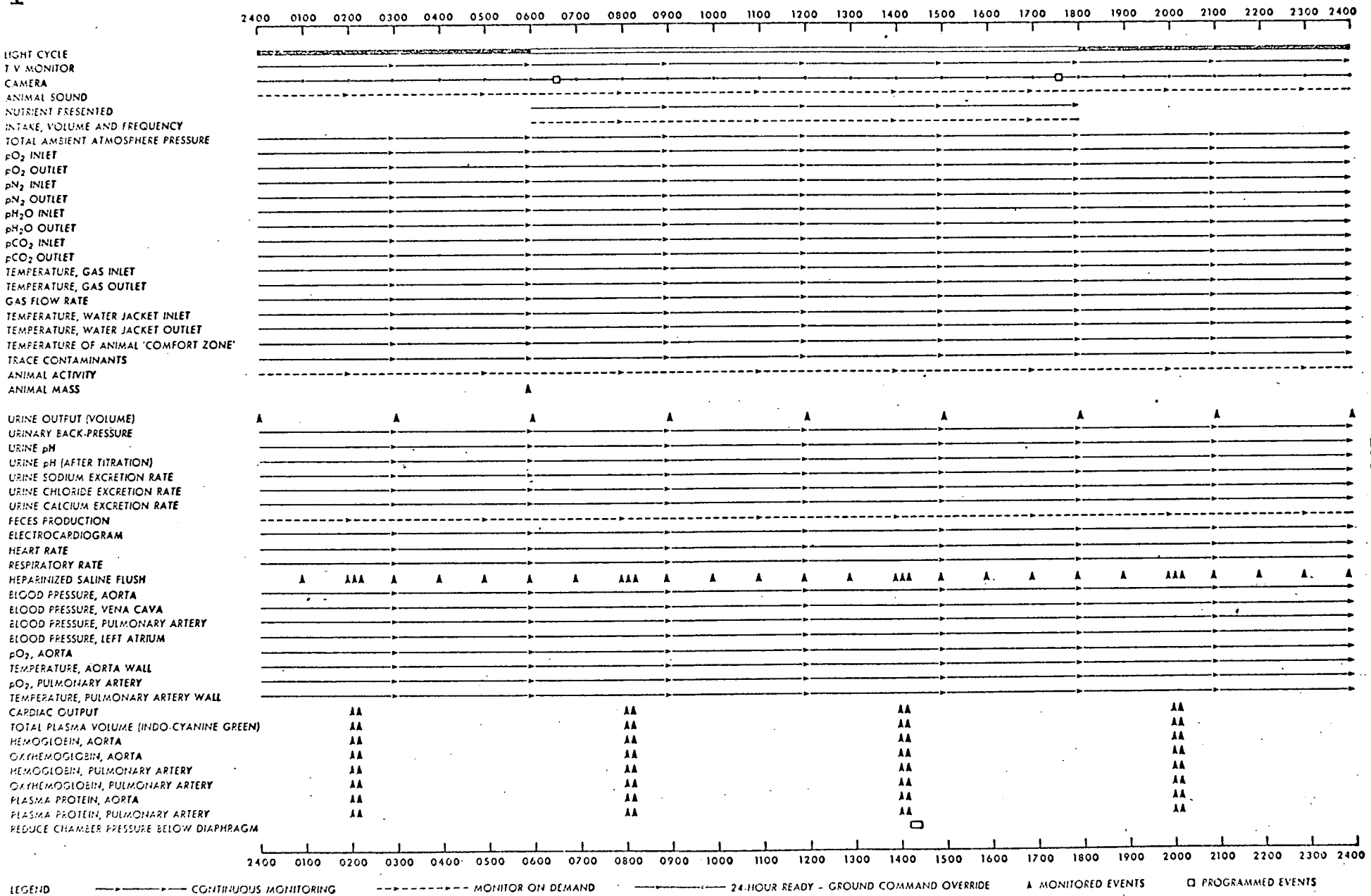
LEGEND
CONTINUOUS MONITORING
MONITOR ON DEMAND
24-HOUR READY - GROUND COMMAND OVERRIDE
MONITORED EVENTS
PROGRAMMED EVENTS

Flight with LBNP

4



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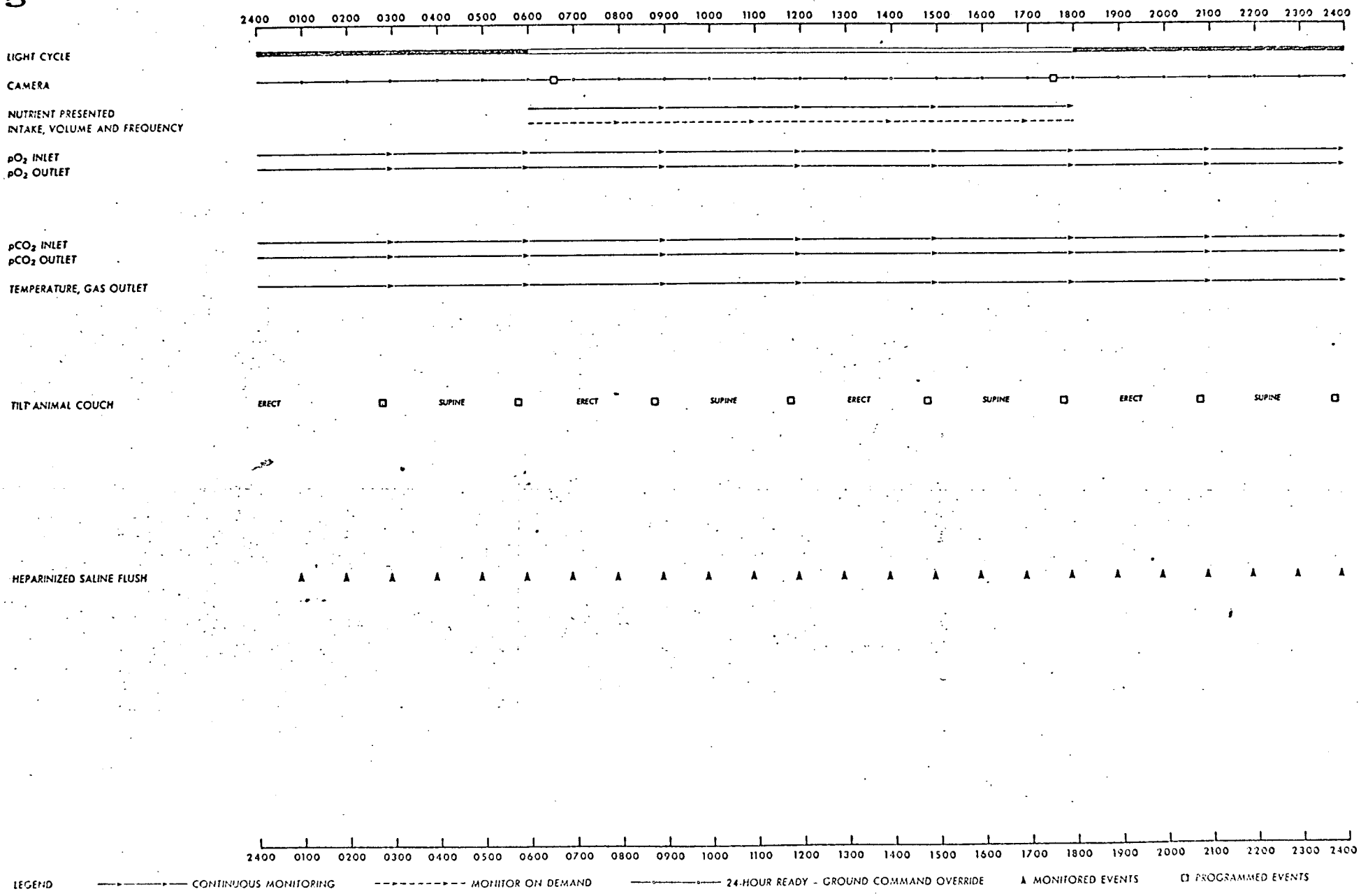
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NUTRIENT PRESENTED
INTAKE, VOLUME AND FREQUENCY
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TILT ANIMAL COUCH
ERECT
SUPINE
ERECT
SUPINE
ERECT
SUPINE
ERECT
SUPINE
HEPARINIZED SALINE FLUSH
2400 0100 0200 0300 0400 0500 0600 0700 0800 0900 1000 1100 1200 1300 1400 1500 1600 1700 1800 1900 2000 2100 2200 2300 2400
LEGEND
CONTINUOUS MONITORING
MONITOR ON DEMAND
24-HOUR READY - GROUND COMMAND OVERRIDE
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PROGRAMMED EVENTS

SECTION X.

APRL

PROJECT DEVELOPMENT PLAN

APRL PROJECT DEVELOPMENT PLAN

Table of Contents

Table of Contents

APRL PROJECT DEVELOPMENT PLAN

1.0 Introduction.

It is proposed that this step in the development of the Automated Primate Research Laboratory (APRL) will translate experiment requirements into suitable engineering concepts for the ultimate execution of a successful space flight experiment based on the approved primate experiment of N. Pace of the University of California, Berkeley.

The above will encompass the feasibility study, development and fabrication of Prototype (Breadboard) hardware and the testing of this hardware to prove the experiment capability. It will include as much Reliability and Quality Assurance as is reasonable and practical within the funding allotted to the program.

1.1 Scope

The APRL program will study feasibility of hardware based on the experiment requirements. Then, in turn, it will carry out development and fabrication of ground test hardware to prove this concept, based on the best information available from previous flight hardware experience of programs already completed by the National Aeronautics and Space Administration.

1.2 Objectives

To develop specific experiment requirements specification which will be used to fabricate and assemble hardware for the carrying out of an intensive biological research test program in order to assure space flight capability.

1.3 Systems

The system to be proven is the primate experiment module that will ultimately become one experiment in the NASA's future space flight experiment program.

This system will consist of the subsystems that follow:

Environmental Control Subsystem
Urine Subsystem
Feces Subsystem
Hemodynamic Subsystem
Nutrient Subsystem
Restraint Subsystem
Data Subsystem
Biomodule Subsystem
Experiment Envelope Subsystem
Electrical Power and Sequential Subsystem

2.0 Management Plan

The plan listed below is that of UCB only. Subcontractors management plan will be added as the contracts are consummated.

2.1 Organization

The organization shown in Fig. 2.1 is that being used in APRL and not for the entirety of the Environmental Physiology Laboratory of the University of California, Berkeley.

2.2 Program Control

Program Control is a group constructed from units within the EPL of personnel, purchasing and accounting, augmented by a Management Information Center. See Fig. 2.2.

2.3 Personnel Requirements

For the first year of this effort requirements are as follows:

Program Manager
Research Physiologist
Administrative Services Officer
Management Information Center Technician
Secretary
Principal Clerk
Senior Typist Clerk

Engineering

Senior Systems Engineer
Senior Mechanical Engineer
Senior Electrical Engineer
Senior Reliability Engineer
Design Draftsman
Scientific Illustrator

Biology

Specialist (Veterinarian)
Assistant Research Physiologist
Assistant Research Biochemist
Assistant Research Nutritionist
3 Laboratory Technician
Animal Caretaker

3.0 Schedules

3.1 UCB Schedules

UCB will establish the initial outline from the present through the point of flight hardware to provide a basis for discussion. It will be as complete in detail as can be developed in one month of schedule study. It will cover from program management level to subcontractor level. Estimates of project funding will be based on the assumption of funding for reasonable continuing progress. Engineering estimates will draw on previous Bioscience flight experience and other relevant sources.

3.2 Subcontractor Schedules

Following the selection of the subcontractor, the subcontractor will review the UCB schedule and any contained in his proposals and immediately advise of any needed corrections those calling for increased time or money. These will be reviewed by UCB prior to any transmittals to NASA Headquarters.

3.3 GFE Schedules

These schedules will be prepared by UCB and NASA as is appropriate.

4.0 Engineering Plan

4.1 General

The Engineering Plan will be developed by the subcontractor after all experimenter research goals have been reviewed and interpreted in the form of hardware requirements. First estimates will be provided based on tabulations of experiments, fuel storage, power and systems requirements.

4.2 Specifications

These will be developed by the subcontractor for review by UCB and NASA Headquarters when appropriate. They shall draw upon existing NASA specifications and information of interest from Biosatellite experience.

4.3 Systems Integration

The APRL subcontractors shall carry responsibility for subsystem integration. All subsystem design groups shall be responsible for continued review and updating of all other interfacing hardware and hold regular review of schedules.

4.3.1 APRL Subsystems

4.3.1.1 Data Logging and Telemetering

The following subsystems will have data logging or telemetering requirements and will be reviewed to assure the best state of the art measurement techniques are incorporated.

4.3.1.1.1 Environmental Control and Metabolic Gas Sensing

4.3.1.1.2 Urine

4.3.1.1.3 Feces

4.3.1.1.4 Hemodynamics

4.3.1.1.5 Nutrient

4.3.1.1.6 Restraint

4.4 Materials

Component subsystem and system materials will be analyzed by the subcontractor. These materials will be analyzed according to the following criteria.

1. Contact compatibility and adjacent materials
2. Vacuum stability when applicable
3. Thermal stability when applicable
4. Corrosion pre- and post-orbital
5. Stress, orbital and vibration
6. Fungus resistance when applicable
7. Cleaning durability, resistance to chemical and thermal processes
8. Storage stability
9. Monkey contact compatibility
10. Feces and urine storage
11. Leakage corrosion potential

UCB will supply initial information and subsequent periodic reviews of all subsystems directly related to the monkey for purposes of material analysis.

4.5 Change Procedures

At any point prior to the final production of the APRL design changes will be considered when initiated by the NASA, UCB or any subcontractor. Changes will be considered in accordance with the following:

1. Necessity of change
2. Research goals
3. Time available
4. Money available

4.5.1 Subcontractor Initiated Changes

Review of potential changes initiated by a subcontractor will depend upon the influence and effect of the change.

1. Changes affecting hardware only with no adverse effect on cost, reliability, performance or time schedule may be made by the subcontractor with written notification and drawing changes to UCB.

2. Changes affecting performance only shall be reviewed by UCB and the subcontractor involved with the change being effected after joint agreement.

3. Changes adversely affecting time schedule, cost, reliability and significant performance shall be effected only after review and approval by UCB and review of other subcontractors involved.

4.5.2 Contractor Initiated Changes

Review of potential changes initiated by UCB will depend on the influence and extent of the change.

1. Changes which have no adverse effect on performance, time schedule, cost or reliability will be reviewed and effected when agreement is reached between UCB and subcontractors involved with written notification to NASA Headquarters.

2. Changes which adversely affect performance, time schedule, cost or reliability will not be effected until review and agreement is first completed by UCB and subcontractors involved followed by approval of UCB.

5.0 Reliability Plan

(See Attachment #1)

5.1 Reliability Program

An APRL Reliability Program Plan will be prepared and submitted in accordance with NPC 250-1.

5.2 Reliability Task Summary

The reliability tasks to be accomplished in support of contract requirements of the APRL project are briefly summarized in the following paragraphs. Details of these tasks are contained in the APRL Reliability Program Plan submitted in compliance with NPC 250-1.

5.2.1 Reliability Program Management

Direct all reliability efforts for the APRL Program; provide liaison with the APRL Program Office and NASA/UCB Reliability; maintain the APRL Reliability Documentation Center; prepare reliability portion of the Monthly Technical Progress Reports; prepare Reliability Program Schedule; maintain cost and technical accomplishment records; conduct failure close-out meetings with NASA/UCB; plan and direct field reliability activities; prepare reliability activities; prepare portion of the Final Project Report.

5.2.2 Reliability Program Plan Preparation

Prepare and publish formal APRL Reliability Program Plan; maintain a master copy of the Plan including all changes; prepare criteria for and follow through with Plan revisions.

5.2.3 Reliability Management Matrix

Develop matrix for a Spacecraft including scheduled events for inclusion in the Reliability Program Plan; maintain matrix weekly; publish matrix monthly and include in the Monthly Technical Progress Report.

5.2.4 Supplier and Subcontractor Control

Evaluate the basic design concept and mission function of the Supplier* Furnished Components to determine the reliability program elements to be

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* Supplier - designates both Major Subcontractors and Suppliers of Mission Critical Components.

required of Suppliers of components critical to mission success.** Prepare and assist in negotiating the Supplier Reliability Requirements (SRR Documents) to ensure technical and cost compatibility between UCB and the Supplier.

Conduct surveys to evaluate Supplier reliability potentials and capabilities prior to award of contract. Maintain records of subcontractor and supplier reliability performance.

5.2.5 APRL Specifications

5.2.5.1 Specification Preparation

Prepare technical data in co-ordination with other engineering operations for the preparation and control of all Engineering Specifications for Systems level, subsystem level, Component and Aerospace Ground Equipment Specifications.

5.2.5.2 Review and Sign-Off

Review and approval of all Design Specifications to assure compliance with anticipated mission events, environmental profile, test criteria, safety margins, derating factors, and apportioned reliability goals.

5.2.5.3 Alteration Notices (AN's)

Prepare Alteration Notices (AN's) for all specifications. Attend Design Change Board meetings for the approval of AN's to maintain program requirements and promote a high level of program consistency.

5.2.5.4 Qualification Testing Approval

Attend Integrated Test Program Board meetings to grant approval for the test requirements section and related parts of all specifications for the qualification testing of all components, assemblies, and systems.

** Mission Critical Components - Include flight hardware, Aerospace Ground Equipment and compatibility between these and Government Furnished Property (GFP).

5.2.6 Reliability Prediction

5.2.6.1 Reliability Estimates

Prepare reliability block diagrams, mathematical models, reliability estimates and apportionments; prepare continuously updated reliability estimates and reapportionments and Reliability Estimate Analysis Reports in accordance with the Reliability Program Plan.

5.2.6.2 Reliability Figure of Merit Analysis (RFMA)

Prepare RFMA's and reapportionments in accordance with the Reliability Program Plan; prepare reports for each RFMA and resulting reapportionment. The RFMA includes Failure Mode, Effect and Criticality Analyses. Recommendations are submitted to the concerned Design Engineer, such as selection of most reliable utilization of electronic and electromechanical parts consistent with program constraints, plus other as outlined in the Reliability Program Plan.

5.2.6.3 Contingency Analyses

Supply failure mode and effect information in support of the APRL Contingency Analyses.

5.2.7 Design Review Program

5.2.7.1 Design Review Planning

Prepare a detailed APRL Review Check List; prepare a design review schedule indicating those items which will have an informal review (no pre-design review package issued), those items which will have a formal review (a pre-design review package issued), and the scheduled date for each review of each item.

5.2.7.2 Informal Design Review

Conduct informal design reviews and issues reports in accordance with the Reliability Program Plan. Design Review meeting minutes are prepared by UCB.

5.2.7.3 Formal Design Review

Conduct formal design reviews in accordance with the Reliability Program Plan; submit a design review package to NASA/UCB at least 10 working days prior to the Design Review Meeting; submit Design Review Action Items Status Forms to NASA/UCB at least 5 working days following the Design Review Meeting; include updated Design Review Action Item Status in the Monthly Technical Progress Report; submit minutes of the Design Review at least 15 working days following the Design Review Meeting; follow-up on all action items.

5.2.7.4 Final Project Report

Prepare a report and critique of Design Review Program results for inclusion in the Final Project Report.

5.2.8 Failure Reporting Analysis

5.2.8.1 Failure Reporting

Review and classify for the reliability effects all reported failures. Update and disseminate monthly the change sheets only to the APRL Failure Summary reports, and issue quarterly, a revised complete Failure Summary Report.

5.2.8.2 Failure Analysis

Perform a failure analysis on all failures; prepare Failure Analysis Reports and Failure Analysis Follow-up Reports; secure corrective action; determine failure close-out documentation requirements and secure documentation. The latter is integrated with NASA/UCB for their review, approved close-out, or open with risk statement.

5.2.9 Parts Program

5.2.9.1 Selected Parts List

Prepare and maintain the APRL Selected Parts Lists and Substitute

Parts Qualification and NASA/UCB Parts Review Status List. Only parts on the APRL AVE and AGE Selected Parts Lists will be used.

5.2.9.2 Parts Application Reviews

Perform Parts Application Reviews of AVE components in support of Reliability Figure-of-Merit Analyses.

5.2.9.3 Parts Consultation Services

Provide parts consultation services to design engineering.

5.2.9.4 Parts Specifications

Prepare new or revised part specifications and drawings for APRL parts to program requirements.

5.2.9.5 Part Evaluation Program

Prepare as an input to the Integrated Test Program a parts evaluation (qualification) test program for those parts on the Spacecraft and AGE Selected Parts List for which additional part evaluation (qualification) data is required; prepare test specifications, procure parts, conduct or monitor tests; prepare reports.

5.2.10 Qualification

5.2.10.1 ITPB Review of Previous Qualification Data

Review all APRL components qualified on previous programs for qualification validity on the APRL program; issue Qualification Compliance Reports.

5.2.10.2 ITPB Review of Test Data

Review APRL qualification test data and issue Qualification Compliance Reports for those items declared qualified.

5.2.10.3 Qualification Status Report

Prepare, maintain, and issue the APRL Qualification Status Report once every quarter.

5.2.10.4 ITPB Review of Design Changes

Design changes to the components are reviewed on a continuous basis by the ITPB Chairman. Significant changes, e.g., non-interchangeable Class I changes, are reviewed by the Board to determine effect on Qualification status of the component.

5.2.15 Standard Program

As a base for the APRL program, maximum use will be made of the standards which have already been generated by NASA.

5.2.15.1 Continuously analyze standards and new design modifications for application of new and revised standards.

5.2.15.2 Prepare new and revised materials and process specification and standards which are inadequately defined.

5.2.15.3 Review and analyze workmanship and detailed soldering requirements for compliance with MSFC - PROC-158B and MAFS STD-154.

5.2.16 Field Reliability

Conduct a Reliability Program in the field to support all pre-launch tests, check-out and launch countdown of the APRL spacecraft. It will include the following: Design Change Board, Configuration identification, failure reporting, failure analysis, failure close-out and support of the eventual Pre-launch Review.

6.0 Quality Assurance

The APRL Quality Assurance Program will be conducted in accordance with the Quality Publication NPC 200-2, dated April, 1962. (See Attachment #1).

Quality documentation will be submitted in accordance with contract data requirements reflected in Table 2-1, Section 2 of this document.

6.1 Management

The manager for the APRL Quality Program is responsible for the quality assurance procedures and plans and the directing thereof to assure that all quality requirements are met. He reports to the Program Manager.

Specific tasks directly assigned include:

(1) Liaison between UCB and subcontractors.

(2) Quarterly Quality Reports.

(3) Maintenance of Quality Program Plan.

(4) Direction of Quality Program.

(5) Local inspection agent.

6.2 Design and Development Control

6.2.1 Drawing and Specification Review

Perform design review of drawings and specifications to assure the inclusion of necessary quality characteristics.

6.2.2 Design Reviews

Participate in design reviews to assure that drawings, specifications, and technical documents contain the requirements for determining and controlling the quality of all items for this contract. At such reviews, quality histories and evaluation of previous designs and experience are used to assure quality type design.

6.2.3 Qualification Tests

Perform or witness qualification tests in accordance with the integrated test plan on components, subsystems and systems.

6.2.4 Identification

Assure necessary identification of materials, processes, and design parameters in design documentation for effective control of parts, components, subsystems, and systems.

6.3 Control of Contractor Procured Material

6.3.1 Supplier Selection

In order to obtain the most competent vendors, data is compiled and analyzed for all proposed vendors. The results of these investigations are integrated with Purchasing, Engineering, and Program Office Personnel. Included in the data are failure histories, results of audits, trip reports, and results of surveys of vendor facilities and capabilities. This data is incorporated into a Vendor Rating System which is maintained on all R&D contracts. Access to this documentation will be provided to NASA upon request.

6.3.2 Procurement Documents

In the procurement phase of the contract, Quality requirements are incorporated directly in the procurement documents. Included in these Quality Assurance Provisions (QAP) are compliance document references (i.e., NPC 200-2, NPC 200-3, etc.) plus special instructions for inspection and testing procedures, data, failure reporting, and corrective action requirements. The type of source inspection (government and/or contractor) is delineated as well as requirements for Receiving Inspection.

6.3.3 Vendor Performance Control

During the vendor fabrication and test cycle, Contractor source inspection (Vendor Surveillance) is performed at the Vendor facilities as required to assure that the quality level is being maintained. Technical assistance to Vendors is provided in problem areas. Throughout the contact, periodic audits will be performed to assess the quality system of the vendor.

6.3.4 Receiving Inspection

Purchased or subcontracted items received by UCB will be inspected upon receipt to assure that the items meet the quality requirements of the

drawings and specifications. Data and certifications will be reviewed. When required, measurements are made and tests performed.

6.3.5 Information Feedback

Maintain a system to feedback to suppliers information necessary for correction of deficiencies detected during any phase of inspection, test assembly, checkout, or use of procured items.

6.3.6 Vendor Rating

Maintain a continuous history file on APRL suppliers and supplier products from which vendors are rated. Vendors with low ratings are warned of their status and its effect on new contract awards.

6.4 Government-Furnished Property

Government-furnished property will be processed and handled in accordance with approved procedures. Failure and deficiency data will be fed back to NASA Headquarters or its representative to prevent recurrence of failures or deficiencies.

6.5 Subcontract Furnished Articles

Control of fabricated material is achieved in the following sequence:

6.5.1 Inspection and Test Planning. Develop and maintain Quality Plans for fabrication, assembly, and test of contractor-fabricated articles. Inspection plans will detail specification references, sequence of assembly and test, requirements for special tooling, gages, fixtures, and test equipment. Plans will also contain information related to data recording, in-process and final inspection controls, and testing.

6.5.2 Acceptance Tests. Perform all necessary tests to assure that components, subsystems, and systems conform to applicable design specifications. After completion of any end item

acceptance test, any unauthorized repair modification or disassembly will be prohibited. In the event that a modification must be authorized due to a change in requirements or damage caused by handling or usage, reinspection and/or retests will be required.

6.5.3 Design Change Control. Participate in the Design Change Board to determine the effects of the proposed change on the quality of the item. Provide necessary modifications to inspection and test procedures and equipment to support the proposed change.

6.5.4 Configuration Verification. Develop and maintain, as part of the Configuration Management and Control System, a complete list (serialized) of all components in each flight vehicle. This list will include the latest drawing revision and AN incorporated in each component and will be based on the Engineering-defined configuration. Upon completion of vehicle testing, this list will be included in the vehicle log book.

6.5.5 Drawing and Change Control. Monitor the system which provides for the control of all drawing and specifications utilized in fabrication, procurement, and inspection of hardware as related to:

(a) Drawings, specifications, and changes thereto.

(b) Removal of drawings, specifications, and changes thereto as they become obsolete.

6.6 UCB Furnished Articles

Hardware components or assemblies designed, developed or built by UCB shall be identified, inventoried and reviewed for quality compliance prior to inclusion in the object hardware list.

6.7 Packing and Shipping

Provide procedures and implementation thereof to assure necessary protection of all articles to prevent damage, loss, deterioration, and degradation, in storage or in transit.

6.8 Marking

Establish and maintain identification and inspection stamp system for assuring an effective control of quality status of all items.

6.9 Reporting

Provide a system for collection and analysis of all troubles, failures, and quality data resulting from testing, inspection, and usage of articles. Provide timely distribution of quality information for corrective action and follow-up across all functions to ensure that problems are being solved and the quality level maintained.

7.0 Manufacturing Plan

7.1 Fabrication and Assembly

All APRL fabrication and assembly, except subcontracted subsystems, will be performed at the UCB, Environmental Physiology Institute's Field Laboratory. This will include the final assembly of the integrated breadboard assembly. Fig. 7-1 illustrates the APRL fabrication and assembly plans.

Sterilization and dust free conditions will not be required at any stage of this breadboard design development except as required by good manufacturing procedure.

7.2 Make or Buy

Table 7-1 indicates lists of the planned "Buy" items and potential vendors. This list will be subject to revision as will be published in revisions of the Project Development Plan.

7.3 Instructions

Special instructions for material care, handling, inventory control and process control will be supplied by UCB. The burden of obtaining these will be the subcontractor's responsibility.

8.0 Test Program

8.1 Test Plans

The APRL Program will utilize three types of tests to provide confidence in the APRL design:

1. Development tests to prove the design concepts are functional and practical.
2. Qualification tests to demonstrate that the hardware, as manufactured to engineering drawings and specifications, can

function as intended by design for that period of time necessary to complete its mission in environments to which it is expected to be exposed.

3. Acceptance tests to demonstrate that the subsystems are compatible.

8.2 Test Schedules

The test schedules are presented in Section 3 of this PDP.

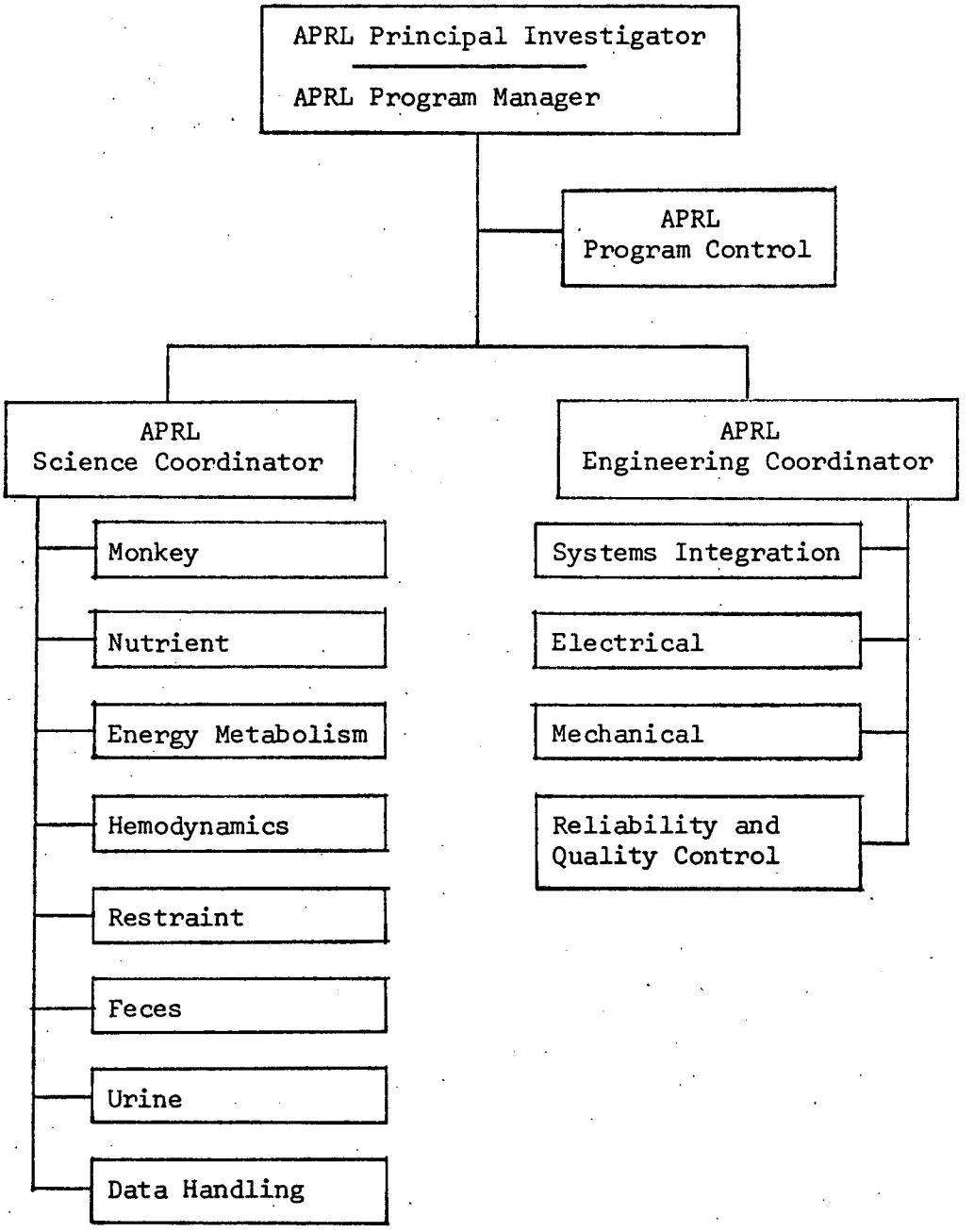

Fig. 2.1. Organization of the APRL Program within the Environmental Physiology Laboratory.

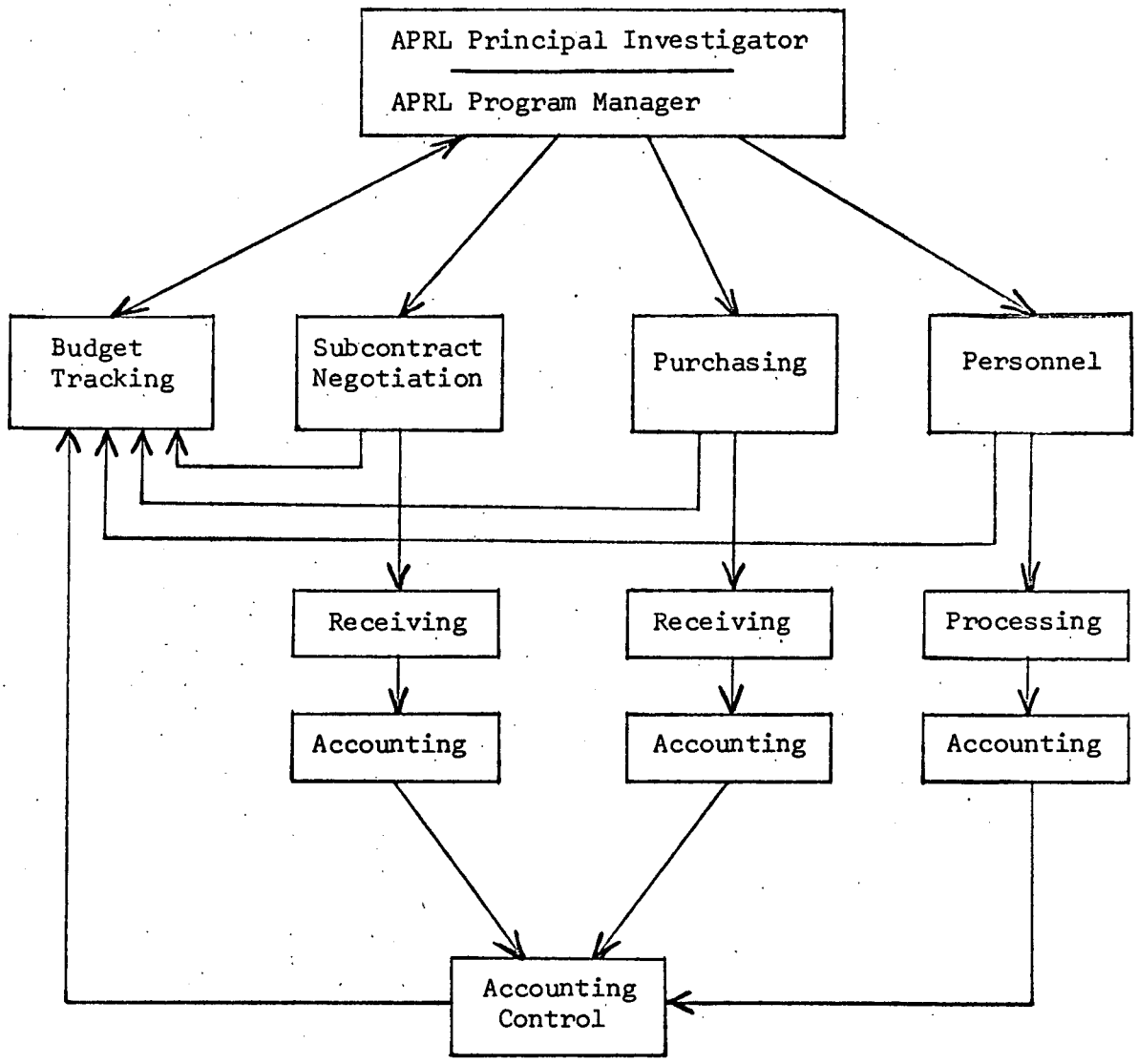

FIG. 2.2. Organization of APRL Program Control (see Fig. 2.1) within the Environmental Physiology Laboratory.